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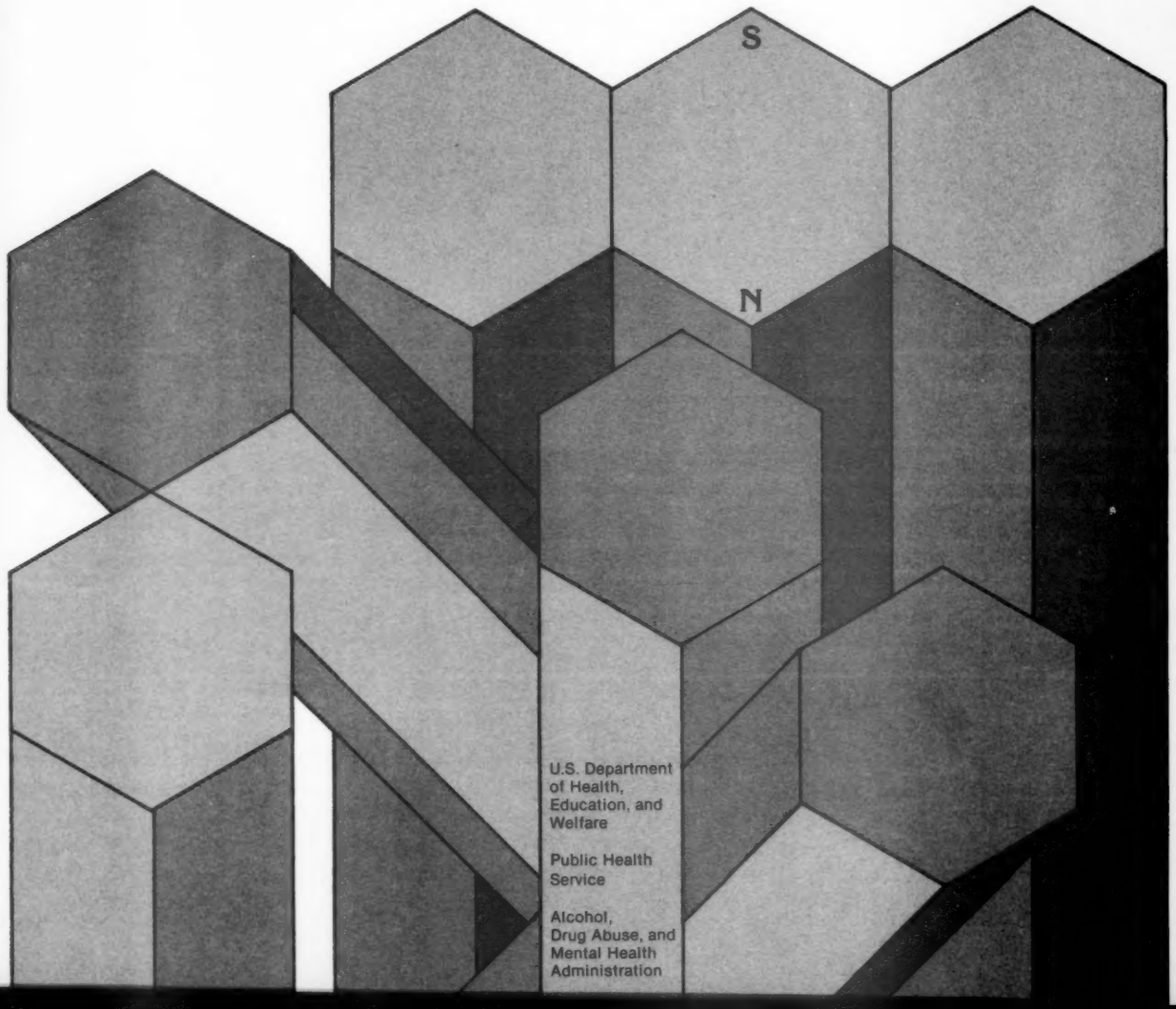

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Carrie Lee Rothgeb, *Editor*
Bette L. Shannon, *Managing Editor*

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

000001 Armstrong, J.; Barlow, R. B. Poultry Research Centre, King's Buildings, Edinburgh EH9 3JN, Scotland **The ionization of phenolic amines, including apomorphine, dopamine and catecholamines and an assessment of zwitterion constants.** British Journal of Pharmacology (London). 57(4):501-516, 1976.

The dissociation constants of many phenolic amines, including benzylamines, phenthylamines, phenylethanolamines, phenylpropylamines, catecholamines and apomorphine were measured by potentiometric titration at 25 degrees centigrade. Measurements were also made with many of their methoxy derivatives and with series of phenolic quaternary ammonium salts. Some compounds were also studied at 37 degrees centigrade. Zwitterion constants were estimated from the pKa values of the phenolic amines and those of their methoxy and quaternary trimethylammonium analogues. Analytical results are tabulated for all samples used unless these have already been published or the samples are of commercial origin. The results confirm the potential importance of ionization in the biological actions of compounds such as apomorphine, dopamine and catecholamines. 19 references. (Author abstract modified)

000002 Baker, G. B.; Raiteri, M.; Bertollini, A.; del Carmine, R.; Keane, P. E.; Martin, I. L. MRC Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Interaction of beta-phenethylamine with dopamine and noradrenaline in the central nervous system of the rat.** Journal of Pharmacy and Pharmacology (London). 28(5):456-457, 1976.

In urethane immobilized rats, the caudate-putamen and thalamus were perfused by means of a push-pull cannula to measure the interaction of beta-phenethylamine (PE) with transport of catecholamines in brain regions rich in dopamine or noradrenaline. Experiments on uptake and release in vitro also were conducted in synaptosome enriched P2 fractions. Results of the in vitro studies indicate that PE caused considerable increase in the release of (ethylamine-1,2-3H)dopamine from striatal synaptosomes while it caused a weaker release of 1(7-3H)noradrenaline from hypothalamic synaptosomes. This interaction with catecholamine transport could account for some of the observations on the stimulant effects of injected PE on locomotor activity. 13 references.

000003 Bartholini, Giuseppe. Research Department, Synthelabo & Co. Ltd, 58, rue de la Glaciere, F-75621 Paris, France **Differential effect of neuroleptic drugs on dopamine turnover in the extrapyramidal and limbic system.** Journal of Pharmacy and Pharmacology (London). 28(5):429-433, 1976.

In gallamine immobilized cats, the caudate nucleus and the necleus accumbens septi were perfused by means of a push-pull cannula and dopamine was measured in the perfusate. Chlorpromazine (10mg/kg to the minus one power) and clozapine (20mg/kg to the minus one power), administered intravenously, enhanced the release of dopamine. The effect of chlorpromazine was similar in both regions whereas that of clozapine was more pronounced in the nucleus accumbens than in the caudate nucleus. Furthermore, in the rat, sulpiride, clozapine and thioridazine increased the homovanillic acid concentration in striatum and limbic system to a similar extent. However, following probenecid administration, the net effect of these drugs on homovanillic acid accumulation was more marked in the limbic system than in the striatum whereas haloperidol and chlorpromazine had a similar effect in the two regions. It is concluded that, in contrast to haloperidol and chlorpromazine, sulpiride, clozapine and thioridazine may preferentially affect the limbic dopaminergic transmission. This possibly accounts for the fact that sulpiride, clozapine and thioridazine display an antipsychotic action and yet cause less extrapyramidal side-effects than haloperidol and chlorpromazine. 21 references. (Author abstract)

000004 Bassus, Jacques; Pacheco, Henri; Chareire, Martine; Trouiller, Gerard; Leblanc, Andre. Service de Chimie Biologique, Batiment 406, Institut National des Sciences Appliquees de Lyon, F-69621 Villeurbanne, France **/Potential psychotropics XI. Synthesis and pharmacological activity of new butyrophenones with an imidazolidin cycle./** Psychotropes potentiels XI. Synthese et activite pharmacologique de nouvelles butyrophenones a cycle imidazolidine. European Journal of Medicinal Chemistry (Paris). 10(4):367-372, 1975.

New butyrophenones with imidazolidin ring 5 and some analogues with opened ring 6 were synthesized. They present little neuroleptic activity. The opening of the imidazolidin ring 3 into a Schiff's base was studied by spectographic methods. 21 references. (Author abstract)

000005 Dzhorbenadze, R. P.; Bostoganashvili, V. S.; Pinyazhko, R. M.; Kvantaliani, E. K. Akademiya Nauk Gruzinskoy SSR, Tbilisi, USSR **/Study of the stability of phenothiazine derivatives./** Izuchenie stabil'nosti lekarstvennykh sredstv proizvodnykh fenotiazina. Soobshcheniya Akademii Nauk Gruzinskoy SSR (Tbilisi). 81(3):625-628, 1976.

The effects of temperature, ultraviolet rays, and pH of the medium on the stability of phenothiazine derivatives (aminazine, propazine, diprazine, dinezine, triphtazine, etaperazine, and meterazine) were investigated. Solutions were analyzed spectrophotometrically, and powders were studied with a thermograph, enabling study of the kinetics of the processes taking place during heating and cooling. The effects of ultraviolet (UV) rays were investigated with an ultraviolet spectrophotometer. Results showed phenothiazine derivatives to be stable up to 200 degrees C, after which destruction occurs in stages. The endothermic effect at 220 to 250 degrees C was replaced by an exothermic effect at 340 to 400 degrees, and complete decomposition occurred at 650 degrees C. Dinezine and etaperazine were found to be the most thermostable. Photodecomposition was investigated in solutions of 0.1to 5.0mg/ml, and the period of irradiation ranged from 1 to 72 hours. During this time the solutions changed from colorless to dark pink, and the characteristic maximums of light absorption were lost, indicating decomposition. Aminazine had the longest half life (14.7hours of UV irradiation at pH 4.7and 10.5hours at pH 2.0), and triphtazine had the shortest (9.1hours at pH 4.7, and 7.5hours at pH 3.0). 5 references.

000006 Frederickson, Robert C. A.; Schirmer, Elmer W.; Grinnan, Edward L.; Harrell, Carolyn E.; Hewes, Christina R. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Human endorphin: comparison with porcine endorphin, enkephalin and normorphine.** Life Sciences (Oxford). 19(8):1181-1189, 1976.

A report is given of the extraction of a material from human brain obtained at autopsy that has morphine like activity on a mouse vas deferens preparation. This human endorphin behaved similarly on Sephadex G-15 and cation exchange columns as did porcine material, and there were no qualitative differences in pharmacological activity between this material and porcine endorphin or enkephalin. It is stated that further purification of the human material is in progress. These results are said to support further the suggestion that the stereospecific binding sites in opiate responsive species are receptors for an endogenous peptide ligand with a role in brain function. 18 references. (Journal abstract)

000007 Goldstein, M.; Bronaugh, R. L.; Ebstein, B.; Roberge, C. Department of Psychiatry, Neurochemistry Laboratories, New York University Medical Center, New York, NY 10016 **Stimulation of tyrosine hydroxylase activity by cyclic AMP in synaptosomes and in soluble striatal enzyme preparations.** Brain Research (Amsterdam). No.109:563-574, 1976.

Dibutyryl cyclic AMP (dB-cAMP) elicits a concentration dependent stimulation of tyrosine hydroxylase activity in the striatal and mesolimbic synaptosomes. The percent of stimulation is significantly higher in the mesolimbic synaptosomes than in the striatal synatosomes. dB-cAMP and depolarizing agents (ouabain or veratridine) have an additive effect on synaptosomal tyrosine hydroxylase activity, indicating that they stimulate tyrosine hydroxylase activity by different mechanisms. cAMP does not stimulate soluble striatal tyrosine hydroxylase activity unless it is added in combination with ATP and Mg2plus, compounds required for the activity of cAMP dependent protein kinase. The cAMP elicited percent stimulation of soluble tyrosine hydroxylase activity is dependent upon the concentration of added protein kinase and upon the pH of the reaction. dB-cAMP has the same effect on the kinetic state of tyrosine hydroxylase in synaptosomes as cAMP on the soluble tyrosine hydroxylase. The nucleotide does not alter the apparent Km for tyrosine, reduces the Km for the pteridine cofactor and increased the Ki for dopamine. Thus, cAMP increases the affinity of tyrosine hydroxylase for the pteridine cofactor and concomitantly decreases the affinity for the end product inhibition. 29 references. (Author abstract)

000008 Hunt, Walter A.; Dalton, Thomas K. Neurobiology Department, Armed Forces Radiobiology Research Institute, Bethesda, MD 20014 **Regional brain acetylcholine levels in rats acutely treated with ethanol or rendered ethanol-dependent.** Brain Research (Amsterdam). No.109:628-631, 1976.

Single doses of ethanol have a biphasic effect on striatal acetylcholine (ACh) levels in the dissected brains of male rats. Parts excised were: cerebellum, brainstem, hypothalamus, hippocamus, caudate nucleus and cerebral cortex. A reduction is observed at low blood ethanol concentrations, while an elevation is found at high concentrations. This is similar to the biphasic effect of ethanol on catecholamine turnover. The reduction in ACh levels observed in ethanol dependent animals still intoxicated is not present during the subsequent withdrawal syndrome. The role of cholinergic mechanisms in the actions of ethanol on the brain and the development and maintenance of ethanol dependence awaits the results of further research. 13 references. (Author abstract modified)

000009 Husser, J.; Hesse, Ch. Koln, West Germany /**Gas and high pressure liquid chromatography: new techniques for psychopharmacological therapy and research.**/ Gas- und Hochdruckflussigkeitschromatographie: Neue Untersuchungsverfahren in der Psychopharmakotherapie und -forschung. Hippokrates (Stuttgart). 47(1):92-93, 1976.

The uses of gas chromatography and high pressure liquid chromatography for psychopharmacological research are briefly discussed. For gas chromatography test materials must be volatilizable; for high pressure liquid chromatography test materials need only be soluble. The latter process simplifies the preparation of test materials and often obviates the production of derivatives. Both methods permit quick, specific, sensitive, and precise quantitive and qualitative analysis of materials, including closely related materials, using a single test process. These methods have been successfully applied in two main areas of medical research: 1) determining the smallest physiologically effective amounts of vitamins, hormones, and their derivatives in intermediary metabolism; and 2) determining minute levels of drugs in the blood and urine in solving pharmacokinetic problems. High pressure liquid chromatography seems most suitable for tricyclic drugs because of their large molecular size. These techniques can also help clarify the mutual interaction of psychotropic drugs and their metabolic derivatives and the influence of these drugs on neurotransmitters. 11 references.

000010 Ishii, Y.; Yoshikawa, A.; Homma, Masako. Research Laboratories, Nippon Kayaku Co., Shimo, Kita-ku, Tokyo 115, Japan **Effect of dopamine-beta-hydroxylase inhibitors on thermoregulation in reserpine-treated rats.** Neuropharmacology (Oxford). 15(6):359-362, 1976.

Dopamine-beta-hydroxylase inhibitors, disulfiram, diethyldithiocarbamate and FD-008, caused marked hypothermia in rats pretreated with reserpine. The hypothermic action was more prominent in 24 hr than in 48 or 72 hr after treatment with reserpine. The hypothermic action of disulfiram or diethyldithiocarbamate was inhibited by L-dihydroxyphenylalanine, but was not inhibited by pimozide, a dopamine receptor blocker. Brain dopamine and norepinephrine were almost depleted in rats treated with reserpine, but a further significant reduction of norepinephrine or a significant increase of dopamine was not observed following administration of disulfiram. L-dihydroxyphenylalanine increased brain dopamine levels in rats treated with reserpine or reserpine plus disulfiram but did not affect norepinephrine levels. 7 references. (Author abstract)

000011 Kraus, Jean-Louis; Yaouanc, Jean-Jacques; Sturtz, Georges. Universite Unulisite de Bretagne Occidentale, Avenue V. LeGorgeu, F-29283 Brest, France /**The role of N-allyl and N-propargyl analogs in the mechanism of inhibition of flavin-linked enzymes: -- N-dimethyl-glycine oxidase -- N-monoamine oxidase.**/ Role des substituants N-allyl et N-propargyl dans le mecanisme d'inhibition d'enzymes flavoproteiques: -- N-demethylase -- monoamineoxydase. European Journal of Medicinal Chemistry (Paris). 10(5):507-513, 1975.

Some analogs of N.N. distributed glycines with allyl or propargyl groups were prepared and tested as N. N. dimethylglycine oxydase inhibitors. On the basis of a study using isotope techniques it is concluded that these analogs, and pargyline in the case of monoamine oxidase, reinforce the hypothesis of inhibitor mechanism by "booby-trap substrates" for flavin linked oxidases. 22 references. (Author abstract modified)

000012 le Petit, G. F. Institute of Clinical Pharmacology, Medical Academy "Carl Gustav Carus", 8019 Dresden, Germany **Medazepam pKa determined by spectrophotometric and solubility methods.** Journal of Pharmaceutical Sciences. 65(7):1094-1095, 1976.

The pKa of medazepam was calculated from four series of UV absorption spectra of solutions of varied pH, according to the method of Albert and Serjeant (1962), at wavelengths of 233nm, 253nm and 286nm. The pKa was determined to be 6.17. Further determinations were performed by the solubility method reported by Green (1967). The pKa was determined to be 6.19. 4 references.

000013 Melchiorre, Carlo; Pigini, Maria; Gualtieri, Fulvio; Giannella, Mario; Johnson, Howard L. Institute of Organic and Pharmaceutical Chemistry, University of Camerino, 62032 Camerino (MC), Italy **Cyclopentone derivatives related to meprobamate: conformation-activity relationships.** European Journal of Medicinal Chemistry (Paris). 10(6):623-627, 1975.

In order to test the validity of a stereochemical approach to CNS active substances, some cyclopertane derivatives, in which the active groups of meprobamate are frozen into stable configurations, were synthesized. The question of the existence of an element of stereospecificity in the action of this kind of drug is examined. The results obtained from the screening suggest that the pharmacological activity of meprobamate is manifested via an extended conformation which approximates the 1,3-trans ring analog. 10 references. (Author abstract modified)

000014 Narasimhachari, N.; Lin, R.-L. Illinois State Psychiatric Institute, Dept. of Research, 1601 Taylor Street, Chicago, IL 60612 **Structure-activity relationships among desmethyl derivatives of neuroleptics and antidepressants for substrate specificity to indolethylamine N-methyltransferase from rabbit lung.** Psychopharmacology Communications. 2(1):27-38, 1976.

Desmethylperazine (norperazine) and desmethylprochlorperazine (norprochlorperazine), like nor-1-chlorpromazine and nor-2-chlorpromazine, are excellent substrates for indolethylamine N-methyltransferase (INMT) and also inhibit the formation of dimethyltryptamine (DMT) from N-methyltryptamine (NMT). Nortriptyline and protriptyline, antidepressant compounds which like NMT contain a secondary amino group, also serve as substrates for INMT but lack in inhibitory effect on DMT formation. 7 references. (Author abstract)

000015 Simantov, Rabi; Goodman, Robert; Aposhian, David; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Phylogenetic distribution of a morphine-like peptide 'enkephalin.'** Brain Research (Amsterdam). 111(1):204-211, 1976.

A naturally occurring morphine like substance, encephalin, was isolated from calf brain and chemically identified as the same pentapeptide that occurs in pig brain but with four times as much leucine encephalin as methionine encephalin. Also reported is a comparison of encephalin activity and opiate receptor binding in 21 invertebrate and vertebrate species, with which the phylogenetic distribution of encephalin activity closely resembles that of the opiate receptor. The presence of substantial amounts of encephalin in the most primitive vertebrates examined suggests a functional role for encephalin throughout vertebrate evolution. The absence of both opiate receptor binding and encephalin activity in invertebrates suggests that investigators seeking to clarify opiate actions relevant to clinical effects of these drugs should focus their studies on vertebrates. 26 references.

000016 Trulson, M. E.; Jacobs, B. L. Department of Psychology, Princeton University, Princeton, NJ 08540 **Dose-response relationships between systemically administered L-tryptophan or L-5-hydroxytryptophan and raphe unit activity in the rat.** Neuropharmacology (Oxford). 15(6):339-344, 1976.

In contrast to previous reports that L-5-hydroxytryptophan (L-5-HTP) is without effect on raphe unit activity, systemic administration of L-tryptophan or L-5-HTP in anesthetized rats produced similar dose dependent decreases in raphe unit activity, ranging from 0-15% at 10mg/kg to 60-90% at 100mg/kg doses. The dose response curve forms a plateau for doses above 100mg/kg of L-5-HTP or L-tryptophan. Neurochemical studies revealed that administration of varying doses of L-tryptophan or L-5-HTP (10-100mg/kg, i.p.)under conditions simulating those of the unit recording procedure, produced dose dependent increases in forebrain serotonin of up to 42% and 353% for a 100mg/kg dose of L-tryptophan or L-5-HTP, respectively. These data suggest that exogeneously administered L-5-HTP serves as an effective serotonin precursor in central serotonergic neurones. Furthermore, increases in forebrain serotonin levels within the range of normal diurnal changes in brain serotonin metabolism may significantly affect the activity of serotonin containing neurones. 23 references. (Author abstract)

000017 Valenti, Piero; Borraccini, Alberto; Da Re, Paolo; Cima, Lorenzo. Department of Chemistry, University of Pisa, Pisa, Italy **Structure-activity relationships in centrally stimulating xanthone derivatives. Introduction to parts X-XII, and part X. Acridone derivatives.** European Journal of Medicinal Chemistry (Paris). 10(4):387-389, 1975.

Aspects of the structure/activity relationships among the central nervous system stimulating xanthone derivatives 1a-e (N-disubstituted 3-methoxy-4-aminomethylxanthones) are examined in 3 different articles. This article deals with the bioisosteric replacement of the heterocyclic ring oxygen with the NH group, namely the conversion of 1 into the acridone analogues 2a-e. Pharmacological results are presented in the last of the 3 articles. 2 references.

000018 Valenti, Piero; Salvadorini, Silverio; Da Re, Paolo; Cima, Lorenzo. Department of Chemistry, University of Pisa, Pisa, Italy **Structure-activity relationships in centrally stimulating xanthone derivatives. Part XI. Lengthening of the basic chain.** European Journal of Medicinal Chemistry (Paris). 10(4):390-394, 1975.

Aspects of the structure/activity relationships among the central nervous system stimulating xanthone derivatives 1a-e (N-disubstituted 3-methoxy-4-aminomethylxanthones) are examined in 3 different articles. This article takes in account the lengthening of the basic chain, i.e. the preparation of the N-disubstituted 3-methoxy-4-beta-aminoethylxanthones 3a-e as well as the 4-gamma-aminopropyl homologues 4a-e. The possible arrangement of the aminomethyl chain and the methoxy group into a cyclic structure was envisaged with the preparation of the N-disubstituted 1-amino-2,2-dimethyl-1,2-dyhydro-6H-furo-(2,3-c)-xanthen-6-one derivatives 5a-e. Pharmacological results are presented in the last of the 3 articles. 9 references.

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

000019 Bigg, D. C. H.; Purvis, S. R. Imperial Chemical Industries Limited, Pharmaceuticals Div., Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG, England **Muscarinic agonists provide a new class of acaricide.** Nature (London). 262(5565):220-222, 1976.

Known muscarinic agonists were tested for activity against the tick Boophilus microplus, using a strain resistant to organophosphorous insecticides and a susceptible strain, in an effort to find new classes of compounds with high acaricidal activity and low mammalian toxicity. The toxicity and structure of the following compounds are tabulated: arecoline, arecoline methiodide, pilocarpine, oxotremorine, oxotremorine methiodide, tremorine, 1-(4-dimethylaminobut-2-ynyl)pyrrolid-2-one, 1-(4-dimethylaminobut-2-ynyl)pyrrolid-2-one methiodide, pyrimithate, and nicotine. The muscarinic agonists examined are acaricidal, and in some cases are highly potent. It is suggested that this unexploited biochemical lesion may provide a useful starting point for the design of new acaricides. 14 references.

000020 Davis, Michael; D'Aquila, Richard. Yale University School of Medicine, New Haven, CT 06505 **Acute intravenous infusion in freely moving rats through the sagittal and transverse sinuses.** Pharmacology, Biochemistry and Behavior. 4(4):469-472, 1976.

A technique is described which allows drugs to be injected intravenously using the junction of the sagittal and transverse sinuses as the point of entry into the venous system. The procedure is rapid and uses conventional stereotaxic techniques. Subsequent restraint of movement during drug infusion is minimal. Using this method, 15micrograms/kg d-lysergic acid diethylamide produced an increase in acoustic startle (a sensitive index for evaluating drug effects on behavior) amplitide within about 1-2 min which lasted for about 25 min. Results indicate that the junction between the transverse and sagittal sinuses is a feasible site for IV injection of drugs in freely moving rats. This method may be preferable to procedures which involve catheterization of the jugular or tail vein but has not been developed for long-term chronic infusion studies over many days. This would entail some way of firmly attaching the infusion needle to the guide tube during testing but also allowing its removal during intervals between testing, as well as determining whether multiple punctures of the sinus would be possible. 16 references. (Author abstract modified)

000021 Fischer, Edmundo. Facultad de Medicina, Universidad Nacional de Buenos Aires, Buenos Aires, Argentina **/Phenethylamine hypothesis for emotional homeostatis. Depressive states and the action mechanism of antidepressants./** Hipotesis fenetilaminica de la homeostatis timica. Episodios depresivos y mecanismo de accion de las drogas antidepresivas. Neuropsiquiatria (Buenos Aires). 6(1):6-14, 1975.

Fischer's hypotheses on the effects of phenethylamine (FEA) on emotional homeostasis in depressive states, the therapeutic action of antidepressants, and amphetamine induced euphoria, are described. References to research on FEA in the treatment of Parkinson's disease are also mentioned. It is postulated that FEA deposits in the brain during depressed states affect the feedback mechanism, releasing FEA in active form, and that free FEA acts to return the emotional state to normalcy by its stimulating action. It is postulated that under normal conditions the rapid inactivation of FEA by monoaminoxidase inhibitors prevents excessive euphoria and ensures a return to normal emotional homeostasis. Experiments are described indicating the presence of FEA in the brain and the direct stimulating action of FEA. 60 references.

000022 Gillin, J. Christian; Tinklenberg, Jared; Stoff, David M.; Stillman, Richard; Shortlidge, Justine S.; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Saint Elizabeths Hospital, Washington, DC 20032 **5-Methoxy-N,N-dimethyltryptamine: behavioral and toxicological effects in animals.** Biological Psychiatry. 11(3):355-358, 1976.

The behavioral and toxicological effects of 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) in rhesus monkeys, Hampshire sheep, hooded rats, and mice are reported. Three young male monkeys given intravenous injections of 250 micrograms per kilogram or more displayed marked ataxia, decreased spontaneous movement and climbing, unresponsiveness to loud noises, threatening gestures, and observable physiological and motor responses. At higher doses, animals were comatose. Two adult male sheep exhibited dose related effects at doses of 20micrograms per kilogram, and a dose of 1mg/kg was fatal. Rats receiving 8 or 16mg/kg of 5-MeO-DMT displayed shivering, lesions, spasms, prostrate posture on back, blanching of blood vessels in ears and paws, abnormal gait and posture, and unusual behaviors. In mice, LD50 iv was 48mg/kg; subcutaneous, 113mg/kg; and oral, 278mg/kg. It is concluded that 5-MeO-DMT has potent, rapidly appearing effects in the central nervous system of the animals studied. 16 references.

000023 Ginos, James Z.; Cotzias, George C.; Tolosa, Eduardo; Tang, Lily C.; LoMonte, Anthony. Medical Research Center, Brookhaven National Laboratory, Upton, NY 11973 **Cholinergic effects of molecular segments of apomorphine and dopaminergic effects of N,N-dialkylated dopamines.** Journal of Medicinal Chemistry. 18(12):1194-1200, 1975.

The hydrochlorides of several molecular segments of apomorphine and their respective N-methyl and N-n-propyl homologs and N,N-dialkylated dopamine compounds were synthesized and studied for: 1) LD50 in intact mice; 2) stereotypy in intact mice; 3) curving of the body in unilaterally caudectomized mice; 4) rotation in 6-hydroxydopamine lesioned rats, and 5) activation of adenylate cyclase in homogenates of mouse caudate nuclei. Instead of dopaminergic effects some of the compounds showed cholinergic effects. These effects were blocked in atropine pretreated animals. Of the N,N-dialkylated dopamine compounds synthesized, the N-n-propyl-N-n-butyldopamine ranked in all tests as the strongest dopamine receptor agonist and N-methyl-N-n-propyldopamine as the weakest. N,N-dimethyldopamine and 1-(3,4-dihydroxyphenylethyl) piperidine showed no dopaminergic effects. The effectiveness of the dopaminergic agonists depended on the length of the N-alkyl substituents suggesting interactions with hydrophobic regions of the receptor site. 22 references. (Author abstract modified)

000024 Kostowski, Wojciech. Samodzielna Pracownia Psychofarmakologii Instytutu Psychoneurologicznego, Warsaw, Poland **/Predicting psychotropic properties of new drugs on the basis of animal experiments./** Rozpoznawanie wlasciwosci psychotropowych nowych lekow w oparciu o badania doswiadczalne na zwierzetach. Psychiatria Polska (Warszawa). 10(1):33-43, 1976.

Problems encountered in describing the properties of psychotropic drugs on the basis of laboratory tests on animals include the imperfect nature of the tests, and difficulties in interpreting results and in applying results to clinical conditions, especially if the drug evinces behavioral or emotional changes. Several different tests which have been made on animals treated with tranquilizers, antidepressants, sedatives, amphetamines and anti-Parkinsonian drugs are described. It is noted that tranquilizers and antidepressants are the most difficult and complex drugs to analyze, and cause the largest number of side-effects. 7 references.

000025 Lassen, J. Buus; Squires, R.; Petersen, E. A/S Ferrosan, Research Laboratories, Sydmarken 5, DK-2860 Soeborg, Denmark **Neurochemical and pharmacological properties of a new serotonin-potentiating phenylpiperidine derivative FG 4963.** Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):475-481, 1975.

The biochemical and pharmacological properties of the substances (t)trans-3((4-methoxyphenoxy)-methyl)-I-methyl-4-phenylpiperidine (FG-4963), a more potent blocker of neuronal 5HT pump than that of the noradrenaline pump (NA pump) are presented. This derivative is a more selective 5HT potentiator than several of the clinically most used tricyclic antidepressants. The study shows the 50% concentration inhibition of amine uptake into rat brain synaptosomes. FG-4963 inhibited 5HT uptake at about the same concentrations (20-30ng/ml) as chlorimipramine. When doses, doubling the mobility of 5HTP treated mice were given, FG-4963 was more active than chlorimipramine. FG-4963 was inactive in doses up to 5mg/kg relative to the potentiation of NA. NA induced heartrate increase was investigated in pithed rats, and indicated less sympathetic stimulation than that produced by the tricyclic thymoleptics. FG-4963 is less toxic and influences the sympathetic system less than the tricyclic antidepressants. 20 references.

000026 Laudenslager, M. L.; Carlisle, H. J. Physiological Research Lab, Scripps Institution of Oceanography, La Jolla, CA 92037 **Heat-escape behavior in the rat following intrahypothalamic injection of acetylcholine.** Pharmacology, Biochemistry and Behavior. 4(4):369-373, 1976.

The effects of preoptic/anterior hypothalamic injections of acetylcholine on heat escape behavior and hypothalamic temperature were investigated in unrestrained rats implanted with bilateral cannulae. Two types of responses were observed, either a fall in hypothalamic temperature coupled with an increase in behavioral responses to escape heat or a rise in hypothalamic temperature associated with little or no change in behavioral heat escape responses. The fall in hypothalamic temperature observed in one group of rats was significant and was associated with a dose dependent increase in heat escape responding. The rise in hypothalamic temperature noted in the other group of rats was nonsignificant, and the associated behavioral responses were variable. Distinct anatomical differences in cannulae loci between the 2 groups were not apparent. It is concluded that acetylcholine activates the heat dissipating control system of the rat hypothalamus and that the hyperthermic effects of acetylcholine are nonspecific. 24 references. (Author abstract)

000027 Papaioannou, G. Pharmacology Laboratory, University of Athens, 104 Solonos St., Athens, Greece **/New morphine derivatives./** Nouveaux derives de la morphine. European Journal of Medicinal Chemistry (Paris). 11(3):287, 1976.

The preparation of new derivatives of morphine by the action of the appropriate aminoalkyl chlorides on the potassium salts of morphine or hydromorphine or by the action of alkyl isocyanate is discussed. Four general types of formulas are presented to describe the new morphine derivatives. Preliminary pharmacological studies of the CNS action and antitussive actions of the new derivatives was also conducted and compared to the literature. 12 references.

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

000028 Ablad, Bengt; Borjesson, Inger; Carlsson, Enar; Johnsson, Gillis. Department of Pharmacology and Medicine, AB Hassle, Fack, S-431 20 Molndal, Sweden **Effects of metoprolol and propranolol on some metabolic responses to catecholamines in the anaesthetized dog.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):85-95, 1975.

The effects of metoprolol and propranolol on the plasma free fatty acid (FFA) response to intravenous infused adrenaline and noradrenaline and on the blood glucose and lactate responses to adrenaline were studied in anesthetized dogs. Both beta-blockers markedly reduced the plasma FFA response to noradrenaline. Metoprolol differed from propranolol by inhibiting the plasma FFA response to adrenaline significantly less than that to noradrenaline. The lactacidemic effect of adrenaline was somewhat reduced by metoprolol and abolished by propranolol. The slight increase of blood glucose concentration produced by adrenaline was not significantly affected by either blocker. Adrenaline elicited a marked increase of the arterial blood pressure after propranolol treatment, whereas a slight hypotensive effect was observed after administration of metoprolol or in control experiments. The effects of metoprolol could be ascribed to inhibition of adrenergic beta1-receptor mediated actions, while those of propranolol are due to combined beta1-receptor and beta2-receptor blockade. 25 references. (Author abstract modified)

000029 Adams, G. Kenneth, III; Yamamura, Henry I.; O'Leary, John F. Dept. of Environmental Medicine, Johns Hopkins University, School of Hygiene and Public Health, 615 N. Wolfe St., Baltimore, MD 21205 **Recovery of central respiratory function following anticholinesterase intoxication.** European Journal of Pharmacology (Amsterdam). 38(1):101-112, 1976.

The possibility of spontaneous return of central respiratory function (that is, without atropine sulfate therapy) after pinacolyl methylphosphonofluoridate (Soman) intoxication was studied; the relationship of this functional recovery to the return of acetylcholinesterase (AChE) activity was investigated, and the physiological and biochemical effects of Soman were compared to those of isopropyl methylphosphonofluoridate (Sarin). The data indicate that in guinea-pigs the spontaneous return of central respiratory function after Soman or Sarin intoxication is not related to the return of brainstem AChE activity, either through regeneration of the original enzyme or synthesis of new enzymatic protein. It is suggested that spontaneous recovery may depend on the desensitization to acetylcholine (ACh) of certain postsynaptic sites in respiratory areas of the brainstem. The membrane desensitization may be a result of receptor inactivation caused by high concentration of ACh consequent to inhibition of brainstem AChE. Following desensitization, the putative respiratory inhibitory control neurons remain inactive, no longer responding to endogenous release of ACh. This relieves the respiratory neuronal pool from excessive inhibitory input, and normal central respiratory activity is restored. 29 references. (Author abstract modified)

000030 Adams, Jeffrey G.; Nicholls, Paul J.; Williams, Hywel. Welsh School of Pharmacy, University of Wales, Institute of Science and Technology, Cardiff CFI 3NU, Wales **Some derivatives of 2,4-diamino-5-phenylthiazole (amiphenazole).** European Journal of Medicinal Chemistry (Paris). 10(4):425-427, 1975.

To facilitate metabolic studies on the analeptic 2,4-diamino-5-phenylthiazole (Amiphenazole) attempts were made to synthesize 2,4-diamino-5-(p-hydroxyphenyl) thiazole (unsuccessful) and 2,4-dihydroxy-5-(hydroxyphenyl) thiazole (successful) as possible metabolites. The pharmacology of some synthetic intermediates revealed that 2,4-diamino-5-(p-methoxyphenyl) thiazole was a more potent stimulant than Amiphenazole in morphine depressed respiration of rabbits while therapeutic indices were comparable. 2,4-Diamino-5-(p-benzyloxyphenyl) thiazole depressed locomotor activity in mice. 2,4-Dihydroxy-5-(p-hydroxyphenyl)) thiazole did not affect morphine induced analgesia in mice. 11 references. (Author abstract)

000031 Alexander, George J.; Kopeloff, Lenore M. Neurotoxicology Research Unit and New York State Psychiatric Institute, New York , NY 10032 **Audiogenic seizures in mice: influence of agents affecting brain serotonin.** Research Communications in Chemical Pathology and Pharmacology. 14(3):437-448, 1976.

The possible relationship between brain serotonin (5-HT) levels and susceptibility to audiogenic seizures were examined in a strain of inbred audiosusceptible mice and in control mice at intervals from 2 hours to 1 week after treatment with several agents known to modify serotonin metabolism. Although p-chlorophenylalanine produces a gradual decrease in brain serotonin there appears to be no temporal correlation between this effect and the rapid reduction in seizure susceptibility. 5-Hydroxytryptophan (5-HTP) and tranylcypromine produce significant increases in serotonin, but only the former causes a proportional reduction in seizure activity. Reserpine and alpha-propyldopacetamide decrease serotonin levels but only reserpine causes an intensification of seizure activity proportional to serotonin changes. It is suggested that the effects of 5-HTP and reserpine on seizure susceptibility appear to be linked to observed brain serotonin levels; further studies are needed to elucidate the mode of p-chlorophenylalanine. 10 references. (Author abstract modified)

000032 Allonen, H.; Iisalo, E.; Nuortio, L. Dept. of Pharmacology, University of Turku, 20520 Turku 52, Finland **Effect of reserpine, desipramine and phenytoin on digoxin induced arrhythmias and myocardial uptake of digoxin in guinea pigs.** Acta Pharmacologica et Toxicologica (Kobenhavn). 37(1):8-16, 1975.

Digoxin was infused intravenously 27.5mu-g/min to guinea pigs. By means of the ECG doses of digoxin needed to cause ventricular extrasystoles (VES), ventricular fibrillation (VF), and asystole (AS) were determined in a control group without any premedication. Three groups were given a pretreatment with desipramine, phenytoin and reserpine. After AS digoxin concentrations in the heart muscle and in the kidneys were determined by radioimmunoassay. The concentrations of adrenaline and noradrenaline were also determined in these tissues. After reserpine and phenytoin the doses of digoxin needed to induce VF and AS were increased. Desipramine had no effect on digitalis induced arrhythmias. The relative uptake of digoxin in the heart muscle was decreased after all of the three premedications; there was no change in the kidney. The tissue catecholamine concentrations were decreased after reserpine and desipramine, but remained unchanged after phenytoin. The lethal dose of digoxin seemed not to correlate to the myocardial digoxin concentration after different premedications. The mechanism of the uptake in the heart muscle seemed to be different from that in the kidney. There was no correlation between the catecholamine concentration in myocardium and the arrhythmogenic effect of digoxin in the different groups. 25 references. (Author abstract)

000033 Altmann, H.; Ten Bruggencate, G.; Pickelmann, P.; Steinberg, R. Neurologische Klinik der Technischen Universitat Munchen, Mohlstr. 28, D-8 Munich 80, Germany **Effects of GABA, glycine, picrotoxin and bicuculline methochloride on rubrospinal neurones in cats.** Brain Research (Amsterdam). 3(2):337-345, 1976.

A microelectrophoretic study was performed of the actions of GABA and glycine, and of their antagonists on rubrospinal neurones. GABA and glycine depressed antidromic and synaptic potentials, hyperpolarized the cell membrane and increased the membrane conductance. GABA was more effective than glycine. Corticorubral ISPSs and the GABA induced membrane hyperpolarization could be reversed by intracellular application of hyperpolarizing current. Picrotoxin and bicuculline methocholoride antagonized inhibitory GABA actions and the corticorubral IPSP or the corresponding extracellular positive field potential. The hypothesis that GABA is the transmitter of the corticorubral inhibition in the cat is supported. 32 references. (Author abstract modified)

000034 Andersen, Melvin E.; Koppenhaver, Randall E.; Jenkins, Lawrence J., Jr. Toxicology Division, Environmental Biosciences Department, Naval Medical Research Institute, Bethesda, MD 20014 **Some neurotoxic properties of triethylene glycol dinitrate: a comparison with decamethonium.** Toxicology and Applied Pharmacology. 36(3):585-594, 1976.

In a comparison study of triethylene glycol dinitrate (TEGDN) with decamethonium (CID), it was found that the 24hr, ip LD50 of triethylene glycol dinitrate (TEGDN) in rats is 995 (1063-932)mg/kg. The ip LD50 of TEGDN in rats anesthetized with pentobarbital is only 321 (605-170)mg/kg. Significant increases in pentobarbital sleep times were observed in rats pretreated with 50mg of TEGDN/kg ip. Higher doses of TEGDN ameliorated Metrazol toxicity and increased zoxazolamine paralysis times. The peripheral nervous system toxicity of TEGDN was compared to that of decamethonium (C10). Both compounds caused severe tremors and clonic convulsions in vivo, and in vitro both selectively blocked nerve stimulated contractions of the cholinergic rat phrenic nerve diaphragm (PND) preparation, with C10 being 60 times more potent in this respect than was TEGDN. When TEGDN and C10 were applied to PND preparations in combinations, the inhibition of the force of contraction occurred more rapidly and was greater than that expected from either compound applied alone. It appears that TEGDN and C10 act at the same site in vivo in the peripheral nervous system to block cholinergic transmission. 19 references. (Journal abstract)

000035 Aquilonius, Sten-Magnus; Eckernas, Sven-Ake. Department of Neurology, University of Uppsala, Box 573, S-75123 Uppsala, Sweden **Cortical and striatal in vivo uptake and metabolism of plasma choline in the rat: effects of haloperidol and apomorphine.** Acta Pharmacologica et Toxicologica (Kobenhavn). 39(1):129-140, 1976.

The in vivo transport of radioactive chloine (Ch) from plasma into brain and the subsequent metabolism of Ch within the cortical and striatal regions was studied in rats, and the effect of haloperidol and apomorphine on Ch uptake was investigated. Following intravenous injection of a tracer dose of 3H-Ch, blood 3H-Ch is incorporated into parietal cortex at a rate of 1.2% per minute, while the corresponding rate in the striatum is 6.4% per minute. It is suggested that active uptake mechanisms exist for incorporating plasma Ch into brain. Cortical 3H-Ch is converted to Ch metabolites other than acetylcholine (ACh) at a rate of 36% per minute, while the striatal rate is only 6% per minute. It is suggested that 3H-Ch

enters into an ACh available Ch pool within the cholinergic neurones which show the highest density in the striatum. A hypothetical scheme for the fate of brain Ch is presented. After intraperitoneal injection of haloperidol, the quantity of 3H-ACh reaching the cortex is not significantly different from that in controls, but the quantity of 3H-ACh reaching the striatum is markedly reduced. After administration of apomorphine to haloperidol treated rats, the quantity of 3H-ACh reaching the cortex is decreased; that reaching the striatum is increased. These results can be interpreted in the light of a dopaminergic inhibition on intrastriatal cholingergic neurones. 30 references. (Author abstract modified).

000036 Arienti, G.; Gaiti, A. no address **Effects of phospholipid administration on endogenous cerebral phospholipid biosynthesis.** Medicina Psicosomatica (Roma). 20(4):423, 1975.

A report discussing the effects of phospholipid on endogenous cerebral phospholipid biosynthesis was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). It has previously been observed that the addition in vitro of ex novo phospholipids stimulates the rate of lecithin formation in rat brain microsomes initiating from phosphoryl choline (PC) but has no stimulative action if the reaction is begun from cytidinediphosphate (CDPC). It therefore appears that the phospholipids act on the probable limiting step in the biosynthesis of lecithin, that is, in the conversion of PC-CDPC. No such data concerning stimulation was obtained following in vivo administration of ex novo phospholipids. It is concluded, however, that the use of neurohomologous phospholipids in vivo demonstrated the occurrence of a significant increase in phospholipid synthesis. (Author abstract modified)

000037 Asakawa, Takeo; Yoshida, Hiroshi. Department of Pharmacology I, Osaka University School of Medicine, Kita-ku, Osaka 530, Japan **F-induced changes and its reversal by ITP in membrane turbidity and adenylate cyclase activity of chick brain microsomes.** Japanese Journal of Pharmacology (Kyoto). 26(2):233-247, 1976.

The effect of fluoride (as NaF) on adenylate cyclase were studied using homogenates of chick telencephalon. Adenylate cyclase activity increased with incubation time and with the concentration of fluoride ion. The activation by fluoride ion was irreversible and magnesium ion was required in addition to produce the maximum effect. Turbidity of the microsome suspension was also greatly increased by fluoride ion plus magnesium ion. The increase in turbidity was rapidly reversed by ATP, GTP, ITP, UTP, and CTP but only ITP reversed the increase in adenylate cyclase activity induced by NaF plus magnesium chloride. It is suggested that fluoride ion induces a change in the membrane structure which may be reversed by incubation with ITP. 36 references.

000038 Atweh, Samir F.; Kuhar, Michael J. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Effects of anesthetics and septal lesions and stimulation on 3H-acetylcholine formation in rat hippocampus.** European Journal of Pharmacology (Amsterdam). 37(2):311-319, 1976.

The rate of 3H-acetylcholine (ACh) formation from intravenously injected 3H-choline was studied in the rat hippocampus after various treatments which alter the activity of cholinergic septal-hippocampal neurons. Administration of pentobarbital and placement of acute septal lesion reduced the formation of 3H-ACh but did not change 3H-choline content. Chloral hydrate administration reduced the formation of 3H-ACh and also increased 3H-choline content. The chloral hydrate induced increase in 3H-choline occurred also in animals with chronic septal lesions. Electrical stimulation of the septum caused an increase in both 3H-ACh and 3H-choline. Chronic septal lesion caused a reduction in both radioactive and endogenous ACh but did not affect radioactive or endogenous ACh but did not affect radioactive or endogenous choline. These findings suggest that there are multiple pools of choline in the brain and that the precursor pool for ACh synthesis is difficult to measure. Overall, the parameter that best correlated with cholinergic activity was the level of 3H-ACh. Possible mechanisms for this finding are discussed. 32 references. (Author abstract)

000039 Audigier, Yves; Virion, Alain; Schwartz, Jean-Charles. Unite 109 de Neurobiologie, 2ter rue d'Alesia, F-75014 Paris, France **Stimulation of cerebral histamine H2 receptors by clonidine.** Nature (London). 262(5566):307-308, 1976.

The action of clonidine on H2 receptors in the brain was investigated in guinea-pig brain tissue slices. Clonidine induces a concentration dependent accumulation of cyclic adenosine monophosphate (cyclic AMP) in the tissue slices. This effect of clonidine is not altered by the alpha-adrenergic antagonist phentolamine, the beta adrenergic antagonist timolol or the histamine H1 antagonist mepyramine. The histamine H2 antagonist metiamide partially inhibits or completely blocks the effect of clonidine, depending on the concentration of metiamide used. It is concluded that clonidine is a potent agonist of histamine H2 receptors and it is suggested that this effect may be related to the hypotensive properties of clonidine. 10 references.

000040 Austin, James H.; Takaori, Shuji. Department of Neurology, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver, CO 80220 **Studies of connections between locus coeruleus and cerebral cortex.** Japanese Journal of Pharmacology (Kyoto). 26(2):145-160, 1976.

A series of experiments was carried out using cats to clarify the effect that locus coeruleus (LC) stimulation has on synaptic transmission between cortical neurons joining the two cerebral hemispheres. The effects of LC stimulation were determined on the transcallosal potential (TCP) evoked in cerebral cortex on the same side. LC stimulation at 8 volts inhibited TCP amplitude an average of 11%. Rostral LC placements appeared most effective. LC stimulation, without drugs, did not affect the peak latency of the TCP, dl-Propranolol and FLA-63 blocked LC inhibition of the TCP and also increased TCP amplitude per se. Propranolol first increased the latency of the TCP during LC stimulation, then decreased it, while also prolonging the latency of the TCP per se. Phenoxybenzamine increased rather than blocked the LC inhibitory effect, and also increased TCP amplitude. dl-Erythro-dihydroxyphenylserine (DOPS) slightly increased the LC inhibitory effect, and substantially increased TCP amplitude. dl-Threo-DOPS produced somnolence in unanesthetized animals, led to increased norepinephrine levels in cortex and brain stem, and caused cortical potentials to fluctuate widely. A midbrain lesion of the dorsal ascending NE bundle blocked the LC inhibitory effect. LC stimulation alone, or in combination with evoked cortical stimulation, did not affect the interstimulus electrocorticogram or the heartrate. It is suggested that in the transcallosal system of the cortical regions studied, the LC plays mainly an inhibitory role. 30 references. (Author abstract modified)

000041 Bagchi, Sakti P.; Zarycki, Edwin P. Research Division, Marcy Psychiatric Center, Department of Mental Hygiene, State of New York, Marcy, NY 13403 **Catecholamine formation in brain from phenylalanine and tyrosine -- effects of psychotropic drugs and other agents.** Biochemical Pharmacology (Oxford). 24(15):1381-1390, 1975.

A comparative study of phenylalanine and tyrosine as the precursors of cerebral catecholamines was undertaken to clarify the mechanisms of catecholamine formation from two types of tyrosine molecules and to examine the effects of psychotropic drugs on brain catecholamine formation. Subcellular fractions of brain regions were incubated with a mixture of 14-phenylalanine and 3H-tyrosine. The ratio of 14C to 3H in the isolated catecholamines (R(CA)) and tyrosine (R(TY)) was determined and taken as a measure of the divergence between the isotope ratio in tyrosine and that in the catecholamines. The experiments indicated that the rate of phenylalanine hydroxylation, the R(CA) value and the R(CA)/R(TY) value may be characteristic properities of specific brain regions. Several physical or chemical agents were found to have profound effects not only on he hydroxylation of phenylalanine but also on the R(CA) and R(XA)/R(TY) values . Lowering the incubation temperature decreased the hydroxylation of both the amino acids but favored the relative formation of catecholamines and the formation of the consecutive hydroxylation product catecholamines. In vivo, chlorpromazine, amphetamine, apormorhine, and morphine were observed to either stimulate or inhibit the formation of catecholamines from phenylalanine following intraventricular administration. The results suggest that: 1) the tyrosine that is formed in vitro from phenylalanine in brain tissue is not freely miscible with the endogenous free tyrosine; 2) the hydroxylation characteristics of the phenylalanine derived tyrosine may be distinctly different from that of the free endogenous tyrosine; and 3) phenylalanine hydroxylation may be sensitive to some psychotropic drugs in vivo. 19 references. (Journal abstract modified)

000042 Banerjee, Anuradha; Poddar, Mrinal K.; Saha, Subhash; Ghosh, Jagat J. Department of Biochemistry, Calcutta University, Calcutta 19, India **Effect of delta9-tetrahydrocannabinol on monoamine oxidase activity of rat tissues in vivo.** Biochemical Pharmacology (Oxford). 24(15):1435-1436, 1975.

The effects of both acute and chronic administartion of delta9 tetrahydrocannabinol (THC) on monoamine oxidase (MAO) in rat blood platelets and in mitochondria from whole brain, hypothalamus, and heart were studied in order to verify whether THC influences biogenic amine levels. THC was injected into male albino rats, and the animals were sacrificed after 6 hrs to study the long-term effect of THC; the treatment was continued for 21 days, and the rats were sacrified 6 hrs after the last injection. The results showed that: 1) THC, both at low and high doses, increased the activity of MAO in blood platelets and in whole brain, hypothalamus, and heart mitochondria but has no effect on MAO activity in liver and kidney mitochondria; and 2) after treatment with THC for 21 days the mitochondrial MAO activties of whole brain and hypothalamus were markedly increased, whereas in liver, kidney, heart and blood platelets, the stimulatory effects were not as great. Also observed was a significant increase in the activity of hypothalamic MAO induced by both acute and chronic administration of THC. It is suggested that the central monoamine neurons are an important site of action of THC. 18 references.

000043 Barker, Jeffery L. Behavioral Biology Branch, National Institute of Child Health and Human Development, Bethesda, MD 20014 **CNS depressants: effects on post-synaptic pharmacology.** Brain Research (Amsterdam). 92(1):35-55, 1975.

The effects of five anesthetics (chloralose, chloroform, ethanol, pentobarbital, and urethane) and one anticonvulsant (diphenylhydantoin) were studied on the membrane properties, and postsynaptic responses of crustacean neuromuscular junction preparations and molluscan neurons to putative transmitters and peptides. In crustacean preparation, pentobarbital selectively depressed in a dose dependent manner, by postsynaptic, Na plus dependent, depolarizing responses to the putative transmitter, glutamate without altering postsynaptic Cl minus dependent inhibitory responses to the putative transmitter gamma-aminobutyric acid. All agents selectively depressed the depolarizing Na plus/K plus dependent postsynaptic responses of the mollusk neurosecretory cell to ACh in a dose dependent, reversible manner appreciably altering the cell's membrane properties. None of them altered hyperpolarizing K plus dependent responses to dopamine and glutamate on the neurosecretory cell, nor did they affect induction or enhancement of BPP activity by the vertebrate peptide vasopressin on this cell. Overall findings suggest that much of the depression of neuronal excitability observed with these CNS depressants is due to a selective postsynaptic depression of the NA plus/K plus dependent conductance mechanism, coupled to postsynaptic receptors. Depression of axonal conduction also contributes to the effects seen in inverse relation to the hydrophobicity of the agent. 70 references. (Author abstract modified)

000044 Barreca, T.; Gianrossi, R.; Masturzo, P.; Polleri, A.; Rollandi, R. no address **Effect of hypothalamic phospholipids on prolactin incretion.** Medicina Psicosomatica (Roma). 20(4):423, 1975.

The role of purified hypothalamic phospholipids on prolactin incretion was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). It is hypothesized that the principal regulatory mechanism of the hormone incretion is dependent on a dopaminergic effect. Experiments showed a suppressive effect of hypothalamic phospholipids on prolactin incretion both in basal conditions and during hormone secretion stimulated previously by chloropromazine. (Author abstract modified)

000045 Baxter, Bruce L.; Gluckman, Melvyn I.; Scerni, Rosemary A. Wyeth Laboratories, Inc., Box 8299, Philadelphia, PA 19101 **Apomorphine self-injection is not affected by alpha-methylparatyrosine treatment: support for dopaminergic reward.** Pharmacology Biochemistry and Behavior. 4(5):611-612, 1976.

The hypothesis that the reinforcing activity of apomorphine is mediated via the release of norepinephrine (NE) was examined in rats. The pattern of self-injection of apomorphine by the animals was studied before and after reduction of brain levels of NE and dopamine (DA) by parenteral administration of the tyrosine hydroxylase inhibitor alpha-methylpratyrosine of amphetamine was also studied in order to indicate indirectly whether or not the AMPT regimen was effective in altering brain catecholamine levels. Pretreatment wtih AMPT at doses which markedly alter the self-injection of amphetamine does not alter the self-injection of apomorphine. It is suggested that the self-injection of apomorphine (reinforcing activity) is produced via the direct activation of DA receptors rather than by the release of either NE or DA. 11 references. (Author abstract modified)

000046 Belvedere, G.; Pantarotto, C.; Rovei, V.; Frigerio, A. Istituto di Ricerche Farmacologiche "Mario Negri," Via Eritrea 62, 20157 Milan, Italy **Identification of 10,11-epoxide and other cyclobenzaprine metabolites isolated from rat urine.** Journal of Pharmaceutical Sciences. 65(6):815-821, 1976.

Cyclobenzaprine (40mg/kg ip) was administered to rats, and six urinary metabolites of this drug were identified using thin layer chromatography, gas liquid chromatography, and mass spectrometry. They were the 10,11-epoxide, the N-oxide, the desmethyl derivative, the hydroxylated and desmethylhydroxylated compounds, and the N-oxide hydroxylated at the 10-position or 11-position. Mass spectrometric analysis confirmed their structures. 9 references. (Author abstract modified)

000047 Bender, David A. Cortauld Institute of Biochemistry, Middlesex Hospital Medical School, London W1P 5PR, England **The effects of chlorpromazine on serum tryptophan, brain tryptophan uptake and brain serotonin synthesis in the rat.** Biochemical Pharmacology (Oxford). 25(15):1743-1746, 1076.

In order to attempt to differentiate between drug induced and abnormalities due to the schizophrenic syndrone in patients, the effects of chlorpromazine on serum tryptophan and brain serotonin synthesis were assessed in rats. Following intraperitoneal injection of single dose of chlopromazine to rats, serum total tryptophan fell significantly, as did the concentration of serum total amino acids. At the same time there was a decrease in the binding of tryptophan to serum albumin, which was not attributable to any change in serum of chlorpromazine (over 10 days), serum tryptophan returned to normal within 4 days, as did the binding of typophan to serum albumin. However, serum total amino acid concentration remained depressed for at least 10 days, returning to the control level immediately on cessation of administration of the drug. Cessation of chlorpromazine administration had no effect on serum tryptophan concentration or binding to serum albumin. Studies on brain tryptohan uptake and serotonin accumulation showed an increase in brain serotonin pool size following single or repeated chlorpromazine adminstration. Although serotonin accumulation was significantly correlated with tryptophan uptake into the brain, the increase in serotonin per unit increase in brain tryptophan uptake was less after 11 days repeated chlorpromazine administration than after a single dose. This suggests that some factor other than tyryptophan availability is concerned in regulation of brain serotonin synthesis; this could be feed-back inhibition by serotonin. 18 references. (Author abstract modified)

000048 Benezet, H. J.; Knowles, C. O. Department of Entomology, University of Missouri, Columbia, MO 65201 **Inhibition of rat brain monoamine oxidase by formamidines and related compounds.** Neuropharmacology (Oxford). 15(6):369-373, 1976.

The efficacy of the pesticide chlordimeform or N-(4-chloro-o-tolyl)-N, N-dimethylformamidine, six chlordimeform metabolites, and related compounds as inhibitors of the oxidative deamination of radiocarbon labelled biogenic amines by rat brain monoamine oxidase was examined. The I50 value of chlordimeform with tyramine as substrate was 6.0x10 to the minus fifth M. Inhibition following prolonged preincubation of chlordimeform with monoamine oxidase increased with time, and this was attributed, at least in part, to the formation of the more potent monoamine oxidase inhibitor 4-chloro-o-formotoluidide, a known chlordimeform metabolite and degradation product. 4-chloro-o-formotoluidide was the most potent monoamine oxidase inhibitor examined yielding I50 values of 2.6, 1.5and 3.2x10 to the minus sixth M, with tyramine, dopamine, and serotonin, respectively, as substrates. The N-demethyl (demethylchlordimeform) and N-didemethyl chlordimeform metabolites gave I50 values with tyramine of 3.3and 7.5x10 to the fifth M, respectively. Three additional metabolites, 4-chloro-o-toluidine, 5-chloroanthranilic acid, and N-formyl-chloroanthranilic acid, were weak inhibitors with I50 values of 1x10 to the minus fourth or higher. The other formamidine compounds also inhibited the oxidative deamination of tyramine; I50 values ranged from 9.3x10 to the minus fifth to 7.5x10 to the minus sixth M. Lineweaver-Burk plots revealed that chlordimeform, demethylchlordimeform, and 4-chloro-o-formotoluidide were competitive inhibitors of the oxidative deamination of beta-phenylethylamine, tyramine, dopamine, tryptamine , and serotonin. Inhibition was reversible since activity was restored by washing. 18 references. (Author abstract)

000049 Benuck, Myron; Marks, Neville. Research Institute for Neurochemistry and Drug Addition, Rockland Research Institute, Ward's Island, New York, NY 10035 **Differences in the degradation of hypothalamic releasing factors by rat and human serum.** Life Sciences (Oxford). 19(8):1271-1276, 1976.

A study shows that rat serum is two to to five fold more active than human serum in cleaving the three hypothalamic releasing hormones, luteinizing hormone releasing hormone (LH-RH), thyrotropin releasing hormone (TRH), and somatostatin. LH-RH was degraded by two distinct enzymatic mechanisms: endopeptidase cleavage and C-terminal cleavage. The C-terminal cleaving enzyme was active in rat serum but present only in trace levels in human serum. These mechanisms were substantiated by the use of suitably substituted analogs. Analogs have enhanced biological activity in vivo which correlates well with their decreased rate of degradation. Degradation of TRH and somatostatin is summarized. It is suggested that a better understanding of the mechanisms of breakdown can facilitate the preparation of derivatives with greater clinical potential. 29 references. (Journal abstract modified)

000050 Bhatacharya, S. K.; Mukhopadhyay, S. N.; Debnath, P. K.; Sanyal, A. K. Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221005, India **Role of 5-hydroxytryptamine in prostaglandin E1-induced potentiation of hexobarbitone hypnosis in albino rats.** Experientia (Basel). 32(7):907-908, 1976.

The effect of prostaglandin E1 (PGE1) on hexobarbitone sleep in rats and the role of 5-hydroxytryptamine (5-HT) turnover in the interaction between the two drugs were investigated. PGE1 potentiated while diclofenac, a prostaglandin synthesis inhibitor, antagonized hexobarbitone hypnosis in rats. PGE1 induced potentiation of hexobarbitone sleep was inhibited by a 5-HT synthesis inhibitor and by a 5-HT receptor blocker, suggesting that this potentiation is 5-HT mediated. It is concluded that hexobarbitone administration in rats triggers a PGE1 induced increase in 5-HT turnover, which in turn contributes to hexobarbitone sleep. 18 references.

000051 Biggio, G.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **GABA receptor activation mediates the decrease of cerebellar cGMP elicited by diazepam. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 22 p.

The action of muscimol and diazepam on cerebellar cGMP content was studied using the decrease of cGMP content of cerebellar cortex as an index of postsynaptic receptor activity. Using this criterion the action of diazepam and muscimol on

000052 cerebellar cGMP content can be differentiated from that of haloperidol or morphine. The antipsychotic and the opiate receptor agonist lower cerebellar cGMP content when given systemically or intrastriatally, but fail to act when injected intracerebellary. In contrast, muscimol and diazepam act when injected parenterally and intracerebellary but not when injected intrastriatally. Since muscimol is a specific GABA receptor agonist, the similarity of the effects of muscimol and diazepam on the cerebellar cGMP content suggests that diazepam actions on cerebellum are mediated by facilitation of synaptic mechanisms involving GABA. This suggestion is corroborated by the finding that intracerebellar diazepam blocks the increase in cerebellar cGMP content elicited by drugs that impair GABA receptor function. 32 references. (Author abstract)

000052 Blank, David L. Code 8357, Naval Research Laboratory, Washington, DC 20375 **Effect of combined reserpine and ECS on electroshock seizure thresholds in mice.** Pharmacology, Biochemistry and Behavior. 4(4):485-487, 1976.

Reserpine combined with electroshock seizure thresholds in mice was investigated. Recent evidence has suggested that electroshock seizure threshold is correlated with levels of brain biogenic amines. Reserpine, a drug that depletes serotonin and norepinephrine, has been shown to decrease seizure thresholds. Electroconvulsive shock (ECS) treatment has been shown to increase amine levels as well as seizure thresholds. Combined reserpine and ECS have been shown to produce an intermediate level of serotonin and norepinephrine, but seizure threshold data for this group is absent. The seizure thresholds for combined treatment is examined and compared with groups treated with reserpine alone, ECS alone, and a placebo control group. The results suggest that if only maximal seizures are considered the reserpine and combined treatment groups do not differ from one another, but do show a lower threshold as compared to ECS or control groups. 13 references. (Author abstract modified)

000053 Blumberg, Jeffrey B.; Vetulani, Jerzy; Stawarz, Robert J.; Sulser, Fridolin. Dept. of Medicinal Chemistry and Pharmacology, College of Pharmacy and Allied Health Professions, Northeastern University, Boston, MA 02115 **The noradrenergic cyclic AMP generating system in the limbic forebrain: pharmacological characterization in vitro and possible role of limbic noradrenergic mechanisms in the mode of action of antipsychotics.** European Journal of Pharmacology (Amsterdam). 37(2):357-366, 1976.

Cyclic adenosine 3',5'-monophosphate (AMP) responses and the effects of adrenergic blocking agents on the cyclic AMP response to norepinephrine (NE), isoproterenol and adenosine in the rat limbic forebrain, the effects of reserpine and 6-hydroxydopamine (6-OHDA) on the NE sensitive cyclic AMP generating system in slices of the rat limbic forebrain and the inhibition by antipsychotic drugs of the specific cyclic AMP response to NE in slices of the rat limbic forebrain were investigated. The results confirm and extend previous observations by Blumberg et al. The results are compatible with the view that the central NE receptor is closely related to, or may be an integral part of, an adenylate cyclase system and that its blockade in the limbic forebrain by antipsychotic drugs may contribute to their therapeutic action. 29 references. (Author abstract modified)

000054 Bodin, Nils-Olof; Borg, Karl Olof; Johansson, Rustan; Ramsay, Carl-Henrik; Skanberg, Inger. Department of Analytical Chemistry and Biochemistry, AB Hassle, Fack, S-431 20 Molndal, Sweden **Tissue distribution of metoprolol-(3H) in the mouse and the rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):116-124, 1975.

The tissue distribution of specifically tritium labelled metoprolol was studied in mice by whole body autoradiography and in rats by determination of unchanged drug and the total pool of metabolites in preselected tissues. The distribution after intravenous administration was characterized by a rapid localization to various tissues e.g. liver, kidney, gall bladder, urinary bladder, salivary glands, Harder's gland, spleen, lungs and adrenals. In the pregnant mouse the drug and/or its metabolites crossed the blood/placenta barrier and moderate concentrations were found in the fetus. Metoprolol was metabolized to a large extent in the rat and after oral administration the total pool of metabolites exceeded the concentration of unchanged drug in the tissues studied. 6 references. (Author abstract modified)

000055 Borg, Karl Olof; Carlsson, Enar; Ek, Lars; Johansson, Rustan. Research Laboratories, AB Hassle, Fack, S-431 20 Moldnal, Sweden **Combined pharmacokinetic and pharmacodynamic studies of metoprolol in the cats and the dog.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):24-30, 1975.

The correlation between the plasma concentration of metoprolol and the heart rate reduction response to isoprenaline in anesthesized cats and exercise tachycardia in conscious dogs was studied. There was a linear relationship between the logarithm of plasma concentration and the pharmacological effect in both species. This relationship was independent of dose level and in the dog it was also found to be independent of the route of administration. The half-life of elimination of metoprolol in plasma was 1.3hours in the anesthesized cat and about 1.7hours in the dog. The ratio between equipotent oral and intravenous doses in the dog was about 3:1 which is in agreement with the bioavailability of metoprolol in this species. 4 references. (Author abstract modified)

000056 Borg, Karl Olof; Fellenius, Erik; Johansson, Rustan; Wallborg, Marita. Department of Analytical Chemistry and Biochemistry, AB Hassle, Fack, S-431 20 Molndal, Sweden **Pharmacokinetic studies of metoprolol-(3H) in the rat and the dog.** Acta Pharmacologica et Toxicologica (Kobenhavn). 39(5):104-115, 1975.

The gastrointestinal absorption, the renal, biliary and fecal excretion, and blood/plasma levels of metoprolol-(3H) in the rat and the dog are described. The compound was well absorbed in both species, about 70% to 100% of the given dose being recovered from the urine within 24 hours irrespective of the route of administration. Low radioactivity was found in feces and bile. The drug was rapidly and extensively distributed to extravascular tissues, the half-life of the distribution process being 5 to 10 minutes. The half-life for the elimination phase in the rat was about 0.6hours and independent of dose and route of administration. The corresponding figure in the dog was about 1.5hours. The systemic bioavailability of metoprolol-(3H) was about 4% in the rat and in the range 20% to 40% in the dog. Since the pharmacokinetic characteristics, obtained by interpreting the blood/plasma curve in terms of a two compartment open model, were rather similar in the dog and in man it is concluded that the dog can serve as a better model for human experiments with this drug than the rat. 18 references. (Author abstract modified)

000057 Bosse, A.; Kuschinsky, K. Max-Plank-Institut fur Experimentelle Medizin, Abteilung Biochemische Pharmakologie, Hermann-Rein-Strasse 3, D-3400 Gottingen, Germany **Alterations of dopaminergic neurotransmission after chronic morphine treatment: pre- and postjunctional studies in striatal tissue.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(1):17-22, 1976.

Repeated morphine administration reversed the acute effects of morphine in rats (e.g. catalepsy and akinesia) and induced symptoms suggesting activation of dopaminergic mechanisms. In morphine withdrawn rats, the potency of intrinsic activity of dopamine in stimulating the synthesis of cyclic AMP in striatal homogenates was not significantly altered. The results suggest that chronic morphine administration to rats increases the dopaminergic neurotransmission in the brain by a presynaptic (prejunctional) mechanism, probably reflecting some kind of adaptation to the acute morphine action, which decreases the dopaminergic neurotransmission. The nigrostriatal dopaminergic system, therefore, seems to be a good model to study acute morphine actions and mechanisms of morphine dependence at the cellular level. 25 references. (Author abstract modified)

000058 Bowery, N. G.; Collins, J. F.; Hill, R. G. Department of Pharmacology, St. Thomas's Hospital Medical School, London SE1, England **Bicyclic phosphorus esters that are potent convulsants and GABA antagonists.** Nature (London). 261(5561):601-603, 1976.

The action of ethyl, isopropyl and pentyl bicyclic organophosphorus (PTBO) compounds is investigated as putative antagonists both of the depressant action of GABA on single neurones in the rat brain and of the depolarizing action of GABA on isolated rat superior cervical ganglion. These bicyclic phosphorus esters produce convulsant seizures in mice without exhibiting an effect on brain cholinesterase activity. The results suggest the convulsant action of the PTBO compounds are related to their ability to antagonize the actions of GABA released as an inhibitory neurotransmitter at synapses in the brain. 14 references.

000059 Bradley, P. B.; Dray, A. Department of Pharmacology, Medical School, Vincent Drive, Birmingham Bl5 2TJ, England **Observations on the pharmacology of cholinoceptive neurones in the rat brain stem.** British Journal of Pharmacology (London). 57(4):599-602, 1976.

The responses of rat medullary neurons to iontophoretically applied acetylcholine (ACh) and other cholinomimetics have been compared and their interactions with cholinoceptor antagonists evaluated. ACh excited most cells but occasionally depressed their activity. Muscarine and the muscarinic agonists methacholine and bethanechol produced prolonged excitation or inhibition of cells whereas nicotine produced prolonged excitations but no inhibitions. Atropine selectively antagonized ACh excitations and both excitation and inhibition of neuronal activity produced by muscarine and muscarinic agonists, but not the excitations produced by nicotine, glutamate or DL-homocysteic acid. It is concluded that excitations of cholinoceptive neurones in the rat brainstem may be mediated by activation of both muscarinic and nicotinic receptors whereas inhibitions are mediated by activation of a muscarinic receptor. 7 references. (Author abstract modified)

000060 Bramwell, G. J.; Gonye, T. Department of Pharmacy, University of Nottingham, University Park, Nottingham, NG7 2RD, England **Responses of midbrain neurones to microiontophoretically applied 5-hydroxytryptamine: comparison with the response to intravenously administered lysergic acid diethylamide.** Neuropharmacology (Oxford). 15(8):457-461, 1976.

An attempt was made to discover why intravenous D-lysergic acid diethylamide (LSD) selectively inhibits the firing rate of raphe neurones recorded in the midbrain of anesthetized rats. Midbrain raphe neurones are more sensitive to the depressant action of microiontophoretically applied 5-hydroxytryptamine than other neurones within the midbrain. When administered in small intravenous doses or at low microiontophoretic currents, LSD slectively inhibited unit firing within the midbrain. Higher intravenous doses or larger microiontophoretic applications also led to the partial inhibition of nonraphe unit firing. It is suggested that LSD may act as an agonist on the inhibitory 5-hydroxytryptamine receptor in addition to being an antagonist at excitatory 5-hydroxytryptamine receptors. 19 references. (Author abstract modified)

000061 Breese, George R.; Cooper, Barrett R. Biological Sciences Research Center, Child Development Institute, University of North Carolina, Chapel Hill, NC 27514 **Effects of catecholamine-depleting drugs and d-amphetamine on self-stimulation obtained from lateral hypothalamus and region of the locus coeruleus.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 190-193).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium, in April 1975, the use of intracranial self-stimulation (SS) behavior in understanding the relationship of catecholamine brain pathways to actions of centrally acting drugs is discussed, based on the effects of catecholamine depleting drugs and d-amphetamine on SS obtained from the lateral hypothalamus and the locus coeruleus. SS was not reduced by 6-hydroxydopamine (6-OHDA) treatments; however, administration of alpha-methyltyrosine (AMT) to rats in which brain dopamine (DA) was reduced produced a larger reduction of SS responding. Reduction of brain norepinephrine (NE) with a dopamine-beta-hydroxylase inhibitor did not alter SS rate. Reduction of brain DA, but not NE, reduced the d-amphetamine induced stimulation of SS responding. The data implicate DA pathways in 6-OHDA, AMT, and d-amphetamine induced effects on SS responding. Conclusions concerning the neurochemical/neuroanatomical basis of SS therefore cannot always be drawn from any drug's actions, because no known dopaminergic pathways exist in the locus coeruleus region. Whether the disruption of SS produced by depletion of brain DA reflects a disturbance in an extrapyramidal integrative system or if a reduction of DA function does in fact block reward remains to be determined. 11 references.

000062 Brezenoff, Henry E.; Mycek, Mary J. Department of Pharmacology, College of Medicine and Dentistry of New Jersey, New Jersey Medical School, 100 Bergen Street, Newark, NJ 07103 **Prevention and reversal of tolerance to barbiturates by intraventricular injection of hemicholinium-3.** European Journal of Pharmacology (Amsterdam). 37(1):125-132, 1976.

Intracerebroventricular (icv) injection of phenobarbital, 800micrograms, or intraperitoneal (ip) injection of hexobarbital, 100mg/kg, into rats results in a loss of righting reflex lasting approximately 15.4minutes and 20.7minutes, respectively. A 40% to 60% reduction in response is obtained following administration of phenobarbital either icv (800micrograms 4 times daily) or ip (80mg/kg/day) for 4 days. Although these treatments also increase hepatic mixed function oxidase activity, this enzyme induction is unrelated to the development of

tolerance to the loss of righting reflex. ICV injection of hemicholinium-3 (HC-3) in doses which reduce brain acetylcholine levels (4-20micrograms) profoundly affect tolerance to the central depressant effect of the barbiturates. Depending upon the time of administration, HC-3 either retards or prevents development of this tolerance. If tolerance is allowed to progress normally, administration of HC-3 on day 4 or 5 returns the duration of the loss of righting reflex towards normal values. HC-3 does not influence either the duration of this response in nontolerant rats or the induction of the hepatic mixed function oxidase activity. It is suggested that brain acetylcholine plays an important role in the development and maintenance of tolerance to the central depressant effects of barbiturates. 22 references. (Author abstract modified)

000063 Brick, J.; Sun, J. Y.; Davis, L.; Pohorecky, L. A. Rockefeller University, New York, NY 10021 **Ethanol and the response to electric shock in rats.** Life Sciences (Oxford). 18(11):1293-1298, 1976.

Recent observations that catecholaminergic neurons are involved in the control of pain sensitivity were investigated as related to the effects of ethanol on mouse electric shock response. Moderate doses of ethanol (2g/kg) were found to have an analgesic effect in rats. When tested with either foot or tail shock, the animals showed progressive analgesia with increasing levels of ethanol in the blood. The vocalization response seemed to be the most sensitive indicator of this parameter. The analgesic effect of ethanol was decreased by half when serotonin levels in the brain were decreased after treatment of animals with p-chloroamphetamine. Inhibition of catecholamine synthesis with alpha-methyl tyrosine had no effect on the analgesic effect of ethanol. 24 references. (Author abtract modified)

000064 Bronaugh, Robert L.; Wenger, Galen R.; Garver, David L.; Rutledge, Charles O. INTERx Research Corp., Lawrence, KS 66044 **Effect of carbidopa on the metabolism of L-dopa in the pigtail monkey.** Biochemical Pharmacology (Oxford). 25(14):1679-1681, 1976.

The effect of the extracerebral dopa decarboxylase inhibitor carbidopa on the metabolism of 3H-L-dopa was examined in the pigtail monkey. In control animals, the eight metabolites measured in urine samples collected for a 24 hour period after the dopa was administered accounts for 89% of the total radioactivity which was injected, while in animals pretreated with carbidopa only 62% of the radioactivity is accounted for by these metabolites. The decrease in radioactivity could be due to increased formation of metabolites which are excreted at slower rates after carbidopa treatment. Excretion of dopamine, dopamine 3-0-sulfate, dopamine 4-0-sulfate and methoxytyramine sulfate is markedly decreased after treatment with carbidopa. Homovanillic acid excretion, 3,4-dihydroxyphenylacetic acid excretion and methoxytyramine excretion are not significantly lowered. Vanillacetic acid excretion increases approximately 14-fold after inhibition of dopa decarboxylase, and it becomes the major metabolite measured. It appears that a difference exists in the sulfate conjugation of dopamine in man and monkey, but it is unclear what factor or factors are responsible for determining which isomer will predominate because the sites of sulfation and enzyme kinetics of the sulfotransferases in the two species are not known. 19 references.

000065 Buckingham, R. L.; Radulovacki, M. Department of Pharmacology, College of Medicine, University of Illinois at the Medical Center, P.O. Box 6998, Chicago IL 60680 **The effects of reserpine, L-Dopa and 5-hydroxytryptophan on 5-hydroxyindoleacetic and homovanillic acids in cerebrospinal fluid, behaviour and EEG in cats.** Neuropharmacology (Oxford). 15(7):389-392, 1976.

The monoamine theories of sleep and wakefulness were tested by administering drugs that deplete or promote the synthesis and storage of 5-hydroxytryptamine (5-HT) and dopamine (DA). The usefulness of determining the levels of metabolites of 5-HT and DA in cerebrospinal fluid from the cisterna magna in correlating changes of brain monoamine turnover with behavior was also investigated. Four hours after injection of reserpine (0.5mg/kg), concentrations of 5-hydroxyindoleacetic acid and homovanillic acid in cerebrospinal fluid increased by 130 and 83% respectively. Eight hours after injection, the first periods of EEG synchronization appeared, coinciding with a decrease in homovanillic acid concentration. Slow wave sleep episodes appeared at 16 hr, at which time the concentration of homovanillic acid approached control levels while the 5-hydroxyindoleacetic acid concentration remained significantly elevated. Administration of l-dihydroxyphenylalanine (50mg/kg) increased homovanillic acid above control levels through 21 hr with a peak increase of 2428% at 4 hr. 5-Hydroxyindoleacetic acid concentration did not change significantly. The animals remained alert with mydriatic pupils. The 9 hr EEG record showed desynchronization in the cortical leads, increased dorsal neck muscle tone and active eye movements. Four hours following administration of 5-hydroxytryptophan (50mg/kg) both 5-hydroxyindoleacetic acid and homovanillic acid increased by 1120% and 75% respectively. Synchronization with short periods of low amplitude appeared during 9 hr of EEG recording. During this time the animals were awake, but demonstrated miotic pupils and recurrent periods of drowsiness. These results suggest that behavior and EEG can be related to changes in brain monoamine metabolism measured in cerebrospinal fluid. Increased metabolism of 5-hydroxytryptamine, as indicated by increased 5-hydroxyindoleacetic acid concentration, correlates with cortical synchronization. Homovanillic acid, the major metabolite of dopamine, increases in waking behavior and EEG desynchronization. 23 references. (Author abstract modified)

000066 Burt, Randall; Freston, James W.; Tolman, Keith G. Department of Internal Medicine, University of Utah College of Medicine, Salt Lake City, UT 84132 **The influence of phenobarbital on biotransformation of 25-hydroxycholecalciferol.** Journal of Clinical Pharmacology. 16(8-9):393-398, 1976.

The influence of phenobarbital on the biotransformation of 25-hydroxycholecalciferol (25-OHD3) to 1,25-dihydroxycholecalciferol (1,25-(OH)2D3) and 24,25-dihydroxycholecalciferol (24,25-(OH)2D3) was investigated in order to clarify the mechanism by which anticonvulsants contribute to the development of osteomalacia. The disappearance rate of 25-OHD3 was virtually the same in the phenobarbital treated group of rats and the control group. Similarly, the appearance rate of 1,25-(OH)2D3 was virtually the same in the treated group and the control group. These data suggest that phenobarbital does not affect the biotransformation of 25-OHD3 to 1,25-(OH)2D3. The implication of this observation is that altered vitamin D metabolism does not account for phenobarbital induced osteomalacia. 21 references.

000067 Cannon, Joseph G.; Gangjee, Aleem; Long John Paul; Allen, Albert John. Division of Medicinal Chemistry and Natural Products, College of Pharmacy, University of Iowa, Iowa City, IA 52242 **Vinyl ethers of choline and congeners.** Journal of Medicinal Chemistry. 19(7):934-937, 1976.

The vinyl ethers of choline and of its alpha-methyl and beta-methyl homologues were prepared to determine their cholinergic effects and to determine whether a separation of the dual physiologic activity (nicotinic and muscarinic) reported for the vinyl ether of choline could be achieved by this modification. A literature method of vinyl transetherification of amino alcohols was studied and modified. The ethyl ethers of choline and of alpha-methylcholine and beta-methylcholine were prepared for comparison with the vinyl ethers. Two independent, unequivocal syntheses of the ethyl ether of beta-methylcholine were accomplished. This study showed that the two literature methods for synthesis of this compound are equivocal, and hence the biological data reported for this compound in the older literature may not be valid. Certain of the ethers showed marked nicotinic or muscarinic activities. 16 references. (Author abstract modified)

000068 Cannon, Joseph G.; O'Donnell, John P.; Lee, Theresa; Hoppin, Charles R.; Long, John Paul; Ilhan, Mustafa; Costall, Brenda; Naylor, Robert J. Division of Medicinal Chemistry, College of Pharmacy, University of College of Pharmacy, University of Iowa, Iowa City, IA 52242. **N-isopropyl derivatives of dopamine and 5,6-dihydroxy-2-aminotetralin.** Journal of Medicinal Chemistry. 18(12):1212-1216, 1975.

Secondary and tertiary amino homologs of dopamine and 5,6-dihydroxy-2-aminotetralin have been prepared, bearing an N-isopropyl group. In peripheral evaluation, certain members of the series exhibited beta-adrenergic agonist effects of lower activity than iso-proterenol. N-Methyl-N-isopropyl-5,6-dihydroxytetralin exhibited marked properties consistent with its being an alpha-adrenergic receptor agonist, and it is concluded that introduction of considerable bulk about the nitrogen of a catecholamine does not a priori destroy alpha-agonist effects. The compounds qualitatively paralleled the effects of dopamine in assays based upon direct intrastriatal administration in rats, although they were less potent than dopamine. 19 references. (Author abstract modified)

000069 Caratsch, C. G.; Waser, P. G.; Spiess, C.; Felix, D.; Walser, J. Pharmakologisches Institut der Universitat Zurich, Zurich, Switzerland **Effect of p-nitrophenyl diazonium fluoroborate on cholinergic mechanisms.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(1):61-68, 1976.

The electrophysiological effect of p-nitrophenyl diazonium fluoroborate (p-NPD) on motor endplates and on hippocampal cholinergic neurons, and to determine the ratio of its affinities to the acetylcholine receptor (AChR) and to the acetylcholinesterase (ACHE) is investigated. The reaults suggest that the biphasic effect depends on the capacity of p-NPD to combine with both the AChE and the AChR. The AChE is first inhibited with low concentrations thereby potentiating the ACh response. At higher concentrations the AChR's are progressively inhibited, too, thereby diminishing the excitability of the postsynaptic membrane up to a complete block. 19 references. (Author abstract modified)

000070 Cardenas, H. L.; Ross, D. H. University of Texas, Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284 **Calcium depletion of synaptosomes after morphine treatment.** British Journal of Pharmacology (London). 57(4):521-526, 1976.

The subcellular locus of the opiate induced calcium depletion in synaptosomal fractions prepared from rat cerebral cortices and the effect of morphine on other cations in subcellular fractions from the brain were studied. It was confirmed that morphone administration in vivo produced a selective decrease in the calcium content of synaptosomal fractions. The effect was prevented by naloxone. After morphone or naloxone, there were no changes in the sodium, potassium and magnesium contents of any of the seven subcellular fractions tested. Since the selective calcium loss was found to occur from fractions similar to those reported to exhibit opiate receptor binding, it is concluded that calcium may play a role in the action of narcotic agonist drugs. 22 references. (Author abstract modified)

000071 Charness, Michael E.; Bylund, David B.; Beckman, Barbara S.; Hollenberg, Morley D.; Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Independent variation of beta-adrenergic receptor binding and catecholamine-stimulated adenylate cyclase activity in rat erythrocytes.** Life Sciences (Oxford). 19(2):243-249, 1976.

The relationship of beta-adrenergic receptor recognition sites and adenylate cyclase during erythrocyte maturation was studied in phenylhydrazine treated rats. Isoproterenol stimulated adenylate cyclase activity in membrane preparations of reticulocyte rich erythrocytes from phenylhydrazine treated rats was nine times greater than in untreated animals. Basal and fluoride stimulated activities were also enhanced two and four fold, respectively. In contrast, the number of beta-adrenergc receptor sites detected by the binding of 125 I-hydroxybenzylpindolol (125I-HYP) was increased only 40% in these same preparations. The dissociation constant of 125I-HYP and the half maximal inhibition of (-)-isoproterenol for receptor binding sites was unchanged. The disporportionately large increase in the activity of the isoporternol sensitive adenylate cyclase, compared with the small increase in the number of 125I-HYP binding sites, indicated that the functions of catecholamine recognition and consequent adenylate cyclase response can vary independently and suggest that the receptor and the cyclase may be autonomous molecular entities. 21 references. (Journal abstract modified)

000072 Chaudhary, Sunil K.; Parmar, Surendra S.; Chaudhary, Mahima; Barthwal, Jayanti P. Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow University, Lucknow 226003, India **Anticonvulsant activity and inhibition of cellular respiratory activity by substituted imidazolocarbamides.** Journal of Pharmaceutical Sciences. 65(7):1010-1014, 1976.

Several 1-(1-aryl-2-mercaptoacetylimidazole)-3-alkyl-carbamides were synthesized and characterized by their sharp melting points, elemental analyses and infrared spectra. These substituted imidazolocarbamides possess anticonvulsant activity, which is demonstrated by the 20-80% protection observed against pentylenetetrazol induced convulsions in mice. The in vitro effects of these carbamides on the cellular respiratory activity of rat brain homogenates were investigated to determine the biochemical mechanism of action for their anticonvulsant activity. The compounds selectively inhibit the nicotinamide adenine dinucleotide (NAD) dependent oxidations of pyrivate, alpha-ketoglutarate, beta-hydroxybutyrate and NADH, but do not affect the NAD independent oxidation of succinate. It is concluded that the anticonvulsant activity possessed by the substituted imidazolocarbamides has no relationship to their ability to inhibit NAD dependent oxidations. 13 references. (Author abstract modified)

000073 Christensen, A. V.; Fjalland, B.; Nielsen, I. Moller. Department of Pharmacology and Toxicology, H. Lundbect &

Co. A/S, Ottiliavej 7-9, DK-2500 Copenhagen-Valby, Denmark **On the supersensitivity of dopamine receptors, induced by neuroleptics.** Psychopharmacology (Berlin). 48(1):1-6, 1976.

In order to expand present knowledge on the pharmacological effects of neuroleptics after prolonged treatment, experiments were conducted to investigate the correlation between induction of receptor blockade and supersensitivity to dopamine agonists, and to investigate the mechanism behind the supersensitivity development. Dopamine receptor blockade (antagonism against methylphenidate induced compulsive gnawing) and supersensitivity to dopamine agonists (occurrence of apomorphine induced compulsive gnawing and enhancement of methylphenidate induced gnawing) induced by eight different neuroleptics administered to mice were measured, and then the influence of teflutixol on potentiating apomorphine induced gnawing compulsion was assessed. A cholinergic/dopaminergic balance was shown to be involved in the manifestation of compulsive behavior during the supersensitivity phase. It is concluded that the dopamine receptor blockade induced by a single dose of neuroleptic agent is a dynamic phenomenon which in the course of time is replaced by an increased sensitivity of receptors to dopamine agonists. 32 references.

000074 Chung, Ho; Brown, David R. Department of Pharmacology, WRAIR, Walter Reed Army Medical Center, Washington, DC 20012 **Mechanism of the effect of acute ethanol on hexobarbital metabolism.** Biochemical Pharmacology (Oxford). 25(14):1613-1616, 1976.

The effect of acute ethanol treatment on hepatic metabolism of hexobarbital (Hb) was studied in the rat. Oral administration of 3g/kg of ethanol (15% w/v) inhibits Hb hydroxylase activity 45-50%. A dose/response relationship is found for ethanol inhibition of Hb metabolism. The overall hepatic microsomal protein content is not affected, but the hepatic cytochrome P-450 level is reduced approximately 42% by this ethanol treatment. Corticosterone (12.5mg/kg, i.p.)inhibits Hb hydroxylase activity 43%. The combination of ethanol and corticosterone treatment further inhibits Hb hydroxylase activity. In vitro, corticosterone inhibits Hb metabolism competitively. Ethanol causes a 3-fold increase in the plasma corticosterone level but has no effect on plasma corticosterone of adrenalectomized rats. Hexobarbital metabolism is not affected by ethanol in adrenalectomized rats. It is concluded that inhibition of hepatic Hb metabolism by acute ethanol was caused by the increased release of corticosterone induced by ethanol. 21 references. (Author abstract modified)

000075 Collard, K. J. Department of Physiology, University College Cardiff, Wales **The effect of chronic lithium administration on stimulation-induced changes in forebrain 5-hydroxyindoles: modification by chlorimipramine.** British Journal of Pharmacology (Basingstoke). 57(3):446P-447P, 1976.

The effects of chlorimipramine on the changes in forebrain 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) production induced by stimulation of the medial raphe nucleus was studied in control rats and in rats which had received lithium for 10 days. The combination of lithium and chlorimipramine alone does not. Chlorimipramine alone decreases 5-HIAA concentration. This effect is abolished by lithium. It is suggested that chlorimipramine reduces production of 5-HIAA by inhibiting uptake of extraneuronally released 5-HT, thereby denying released 5-HT access to intraneuronla monoamine oxidase. The lack of effect of chlorimipramine on the increase in 5-HIAA concentration in the lithium treated animals suggests that the 5-HIAA in these animals is produced primarily from intracellular 5-HT. Lithium does not antagonize the inhibition of uptake by chlorimipramine. It is suggested that lithium antagonizes the effect of chlorimipramine by inhibiting the extraneuronal release of 5-HT by promoting the release of5-HT into the cytoplasm. 1 reference.

000076 Constantinescu, Elisabeta; Hategan, Dora; Tudor, Sanda; Volanschi, D. Institute of Neurology and Psychiatry, Bucharest, Romania **The influence of antiepileptic drugs on some enzymes activity in the brain of mice with audiogenic epilepsy. Note I. The action of phenobarbital, diphenylhydantoin and primidone.** Neurologie et Psychiatrie (Bucuresti). 14(2):119-128, 1976.

The effects of phenobarbital, diphenylhydantoin, and primidone on cytochrome oxidase, alanine aminotransferase, aspartate aminotransferase, and monoamine oxidase activity in the cerebellum, cerebral cortex, hippocampus, anterior brain stem, and posterior brain stem were studied in vivo in mice with genetic predisposition to audiogenic epileptic seizures. The doses administered prevented the occurrence of seizures after acoustic stimuli were presented without producing significant narcotic effects, hypnotic effects, or neurotoxic effects. The changes in enzymatic activity within the various cerebral structures were for the most part minor increases in activity or decreases in activity, depending on the specific brain region examined and the drug administered. The only statistically significant modifications in enzyme activity reported were: 1) decreased alanine aminotransferase activity in the cerebellum following diphenylhydantoin; 2) increased alanine aminotransferase activity in the cerebellum following phenobarbital; and 3) increased monoamine oxidase activity in the posterior brain stem following phenobarbital. It is concluded that no correlation exists between the chemical structures of the anticonvulsant drugs studied and their effects on enzyme function in various structures of the brain. 25 references.

000077 Cools, Alexander R.; Boudier, Harry A. J. Struyker; Van Rossum, Jacques M. Dept. of Pharmacology, University of Nijmegen, Geert Grooteplein Noord 21, Nijmegen, The Netherlands **Dopamine receptors: selective agonists and antagonists of functionally distinct types within the feline brain.** European Journal of Pharmacology (Amsterdam). 37(2):283-293, 1976.

Unilateral injections of agents that are useful tools for differentiating electrophysiologically distinct dopamine receptors within the snail Helix aspersa were given into behaviorally distinct dopamine sensitive areas within the caudate nucleus of cats. Dopamine elicited contralateral head turning is selectively mimicked by apomorphine and selectively inhibited by haloperidol, whereas dopamine elicited homolateral head turning including oro-facial dyskinesias is selectively mimicked by (3,4-dihydroxy-phenylamino)-2-imidazoline and selectively inhibited by ergometrine, piribedil and noradrenaline. These results indicate that the caudate nucleus of cats contains two functionally and pharmalogically distinct dopamine receptors, and that Helix aspersa dopamine sensitive neurons can be used as model for the design of drugs selectively interfering with each type of receptor. The implications of these findings are considered in view of the efficacy of piribedil, levodopa (L-dopa) and neuroleptics in psychomotor diseases in man. 28 references. (Author abstract)

000078 Costa, E.; Trabucchi, M. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeth's Hospital, Washington, DC **Regulation of brain dopamine turnover rate: phar-**

macological implications. In: Friedhoff, A., Catecholamines and behavior. Vol. 1. New York, Plenum Press, 1975. 235 p. (p. 201-227).

The theoretical and technical difficulties encountered when the dopaminergic neurons are studied in vivo to detect how drugs and environment affect brain dopamine turnover rates are discussed. These studies are complicated by the selectivity of drug action in particular brain nuclei. Only an evaluation of a number of simultaneous measurements of dopaminergic reception function and compartmentation in each of the three dopaminergic neuronal systems and the various nuclei that are innervated by them will define the changes caused by various experimental conditions. A review of pertinent studies includes the suggestion that striatal cyclic AMP is a reliable index of the activation of dopaminergic receptor functions. The molecular mechanisms for the regulation of dopaminergic neurons are discussed. Studies on the regulatory striatal enzymes tyrosine hydroxylase (TH) and adenylcyclase are summarized. Comparative studies of dopamine turnover rate, TH activity and striatal cAMP concentrations in animals administred anticholinergics, neuroleptics, morphine and apomorphine are described and interpreted. 73 references.

000079 Cotler, Stanley; Holazo, Alice; Boxenbaum, Harold G.; Kaplan, Stanley A. Dept. of Biochemistry and Drug Metabolism, Hoffmann-LaRoche Inc., Nutley, NJ 07110 **Influence of route of administration on physiological availability of levodopa in dogs.** Journal of Pharmaceutical Sciences. 65(6):822-827, 1976.

The physiological basis for the reduced levodopa bioavailability following oral administration was investigated. Four dogs received single 25mg/kg doses of (14)C-levodopa on three separate occasions in a crossover fashion via hepatoportal catheter, intravenous and oral administrations. Plasma and urine specimens were analyzed for intact levodopa and total radioactivity. The ratios of areas under the plasma concentration/time curves following hepatoportal and intravenous administrations were close to unity, and the shapes of the curves were virtually identical. Following oral administration, however, significant reductions in the areas under the plasma concentration/time curves were observed. These data indicate that the physiologically impaired bioavailability of orally administered levodopa occurs almost exclusively as a result of metabolic degradation within the GI lumen and/or gut wall. 29 references. (Author abstract)

000080 Couch, James R. Laboratory of Neuropharmacology IRP, SMHR, National Institute of Mental Health, St. Elizabeths Hospital, Washington DC 20032 **Action of LSD on raphe neurons and effect on presumed serotonergic raphe synapses.** Brain Research (Amsterdam). 110(2):417-424, 1976.

The effects of lysergic acid diethylamide (LSD) on the postulated excitatory serotonergic synapse originating in the nucleus paragigantocellularis lateralis (NPL) and terminating on pontine and midbrain raphe neurons and on the postulated inhibitory serotonergic synapse in another group of 25 raphe neurons that are inhibited by NPL stimulation were studied in rats. Standard electrophysiological recording techniques were used. The possibility of synaptic block was investigated by testing synaptic efficacy before and after LSD. For the excitatory synapses the number of failed excitations at threshold were counted before and after LSD application. For the inhibitory synapse, poststimulus time histograms of inhibitory response before and after LSD demonstrated the presence or absence of blockade. It is suggested that LSD might have a dual effect on central serotonergic systems, acting to block excitatory 5-hydroxytryptamine (5-HT) synapses and to stimulate inhibitory 5-HT receptors. 25 references.

000081 Crow, T. J. Division of Psychiatry, Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England **Specific monoamine systems as reward pathways: evidence for the hypothesis that activation of the ventral mesencephalic dopaminergic neurones and noradrenergic neurones of the locus coeruleus complex will support self-stimulation responding.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 211-237).

In a paper presented at the First Internationl Conference on Brain Stimulation Reward, Beerse, Belgium, in April 1975, pharmacological and anatomical evidence concerning the hypothesis that activation of specific monoamine pathways supports electrical self-stimulation (SS) behavior is reviewed. It is suggested that although pharmacological finding are generally damaging to the hypothesis that central serotonergic or cholinergic transmission is essential to the rewarding effects of intracranial stimulation, they do not eliminate the hypothesis that central cathecholaminergic transmission is necessary. Attention is drawn to the difficulty in interpreting the effects of drugs which enhance SS responding in neurochemical terms, and it is suggested that the enhancement of responding observed following intraventricular injections of noradrenaline cannot be interpreted as a facilitation of transmission in a noradrenergic reward system. The anatomical evidence of a relationship between SS sites and location of specific monoamine systems is examined, with particular attention to the prediction that if certain systems are directly involved in SS, there should be a close relationship between positive electrode site and location of particular monoamine containing cell body groups in the brainstem. It is suggested that ascending catecolamine systems may fall into three functional groups: 1) rostrally placed groups of dopamine containing cells; 2) the locus coeruleus complex of noradrenaline containing cells in the midpons; and 3) a caudal group. 113 references.

000082 D'Amico, D. J.; Patel, B. C.; Klawans, H. L. Abraham Lincoln School of Medicine, University of Illinois, Chicago, IL **The effect of methysergide on 5-hydroxytryptamine turnover in whole brain.** Journal of Pharmacy and Pharmacology (London). 28(5):454-456, 1976.

The effects of methysergide on concentrations of 5-hydroxtryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in whole brain was examined in a study which also considered the results in terms of the hypothesis that 5-HT receptor blockage causes increased 5-HT turnover. Experiments on guinea-pigs also examined the effect of simultaneous dopaminergic blockage relevant to the action of methiothepin in which haloperidol was given simultaneously with methysergide. Results indicate that methysergide fails to alter 5-HIAA concentrations and does not change 5-HT turnover in the whole brain. It is posited that either methysergide does not act as central 5-HT receptor blocker or that methiothepin elevates 5-HIAA through some other mechanism. 16 references.

000083 Da Prada, Mose; Keller, Hans H. Pharmaceutical Research Department, F. Hoffman-La Roche and Company, Ltd., Basle, Switzerland **Baclofen and gamma-hydroxybutyrate: similar effects on cerebral dopamine neurones.** Life Sciences (Oxford). 19(8):1253-1263, 1976.

A report of a similarity between baclofen and gamma-hydroxybutyrate (GHB) is presented. Baclofen caused an increase in the content of homovanillic acid (HVA) and dopamine (DA) in rat brain 2 to 3 hours after drug injection

without appreciable changes in the level of other monoamines and their main metabolites. Six and eight hours after baclofen, the content of HVA but not that of DA was reduced. Moreover, baclofen initially reduced, but later enhanced, the accumulation of HVA induced by probenecid. The short lasting initial reduction of HVA elevation in probenecid pretreated animals as well as the long lasting decrease of HVA levels in rats injected with baclofen alone may be due to a decreased release and metabolism of DA, probably as a consequence of the blockade of impulse flow in mesolimbic and nigrostriatal DA neurones. The increase in HVA and DA during the first few hours may result from enhanced DA synthesis similar to that known for GHB. This initial rise in HVA probably masks a reduction of HVA to be expected immediately after baclofen injection. The similarity between baclofen and GHB is supported by the finding that baclofen counteracted the increase of HVA occurring after chlorpromazine and D-amphetamine but not that induced by the banzoquinolizine derivative, Ro 4-1284. 40 references. (Journal abstract modified).

000084 Dahl, Svein G.; Refsum, Helge. Institute of Pharmacology, University of Oslo, Blindern, Oslo 3, Norway **Effects of levomepromazine, chlorpromazine and their sulfoxides on isolated rat atria.** European Journal of Pharmacology (Amsterdam). 37(2):241-248, 1976.

The effects of levomepromazine, chlorpromazine and their sulfoxides were studied on spontaneously beating and on electrically driven rat atria in vitro. Levomepromazine, chlorpromazine and levomepromazine sulfoxide produced a dose dependent decrease in the work index of spontaneously beating atria and in the contractile force of electrically driven atria, while chlorpromazine sulfoxide was relatively inactive in these respects. At higher concentrations, levomepromazine sulfoxide caused a pronounced increase in the threshold for electrical stimulation and the effective refractory period. Compared to chlorpromazine, levomepromazine looses less of its cardiodepressive effect through sulfoxidation. 18 references. (Author abstract)

000085 Daly, J. W. National Institute of Arthritis, Metabolism, and Digestive Diseases, National Institute of Health, Bethesda, MD 20014 **The nature of receptors regulating the formation of cyclic AMP in brain tissue.** Life Sciences (Oxford). 18(12):1349-1358, 1976.

Extensive studies of the past 7 years which have provided fundamental information on the pharmacological properties of receptors controlling formation of cyclic AMP in brain slices and homogenates are reviewed. Receptors serotonin, H1-histaminergic and H2-histaminergic agonists, and prostaglandins of the E series are defined and evidence for a glutamate receptor is presented. Extrapolation of such pharmacological data to studies with whole animals should provide important information as to the physiological significance of specific cyclic AMP generating systems to the function of the intact brain. 80 references. (Author abstract modified)

000086 Danielson, T. J.; Petrali, E. H.; Wishart, T. B. Psychiatric Research Division, University Hospital, University of Saskatchewan, Saskatoon, Saskatchewan S7N 0W8, Canada **The effect of acute and chronic injections of d-amphetamine sulfate and substantia nigra lesions on the distribution of amphetamine and para-hydroxyamphetamine in the rat brain.** Life Sciences (Oxford). 19(8):1265-1269, 1976.

Results of a study in which amphetamine and para-hydroxyamphetamine were identified in four rat brain regions after various treatments with d-amphetamine sulfate are presented. The data indicate a rapid and prolonged concentration of para-hydroxyamphetamine into the striatum and olfactory tubercles. Electrolytic lesions placed in the substantia nigra reduced para-hydroxyamphetamine accumulation in the ipsilateral striatum, suggesting that this amine was concentrated into neuronal structures originating in the substantia nigra. 15 references. (Journal abstract)

000087 Danielson, T. J.; Wishart, T. B.; Boulton, A. A. Psychiatric Research Division, University Hospital, Saskatoon, Saskatechewan, Canada S7N OW8 **Effect of acute and chronic injections of amphetamine on intracranial self-stimulation (ICS) and some aryl alkyl amines in the rat brain.** Life Sciences (Oxford). 18(11):1237-1244, 1976.

The effect of amphetamine treatment on the concentration and distribution of aryl, alkyl trace amines (meta and para tyramine and beta-phenylethylamine) and on intracranial self-stimulation (ICS) were investigated in male Wistar rats. A single injection of amphetamine was shown to reduce the para tyramine concentration in the striatum and olfactory tubercles meta tyramine values increased. After chronic treatment, this pattern persisted with respect to meta tyramine in the striatum and para typramine in the olfactory tubercles. In the striatum the para tryamine returned towards the endogenous value. No effect on these two trace amines was observed in the hypothalamus or hippocampus, nor were significant changes noted in any region with respect to beta-phenylethylamine. A direct relationship between para tyramine concentration and amphetamine induced ICS and tolerance was demonstrated. 50 references. (Author abstract modified)

000088 Danielson, Terry J.; Boulton, Alan A. Psychiatric Research Unit, University Hospital, Saskatoon, Saskatchewan S7N OW8, Canada **Distribution and occurrence of amphetamine and p-hydroxyamphetamine in tissues of the rat after injection of d-amphetamine sulfate.** European Journal of Pharmacology (Amsterdam). 37(2):257-264, 1976.

The time course of the p-hydroxyamphetamine (p-OHA) formation and the distribution of amphetamine (AMPH) and p-OHA in the rat, and the cerebral disposition of p-OHA after varying doses of d-amphetamine sulfate were investigated. AMPH entered all organs readily and was rapidly eliminated. p-OHA was rapidly synthesized and it is suggested that the substrate inhibition of hepatic hydroxylating enzymes occurs. In the brain, AMPH was homogeneously distributed between the seven brain regions examined, whereas p-OHA was predominantly concentrated in the striatum. 46 references. (Author abstract modified)

000089 Delini-Stula, A.; Meier, M. Research Department, Pharmaceuticals Division, Ciba-Geigy Limited, Basle, Switzerland **Inhibitory effects of propranolol and oxprenolol on excitation induced by a MAO inhibitor and reserpine in the mouse.** Neuropharmacology (Oxford). 15(7):383-388, 1976.

Optically active enantiomers of propranolol and oxprenolol were tested for their inhibitor action on locomotor excitation in mice treated with pargyline (75mg/kg, ip) and subsequently with reserpine (5mg/kg, ip). Sotalol and pindolol were also tested for compariosn. All drugs except pindolol demonstrate dose dependent and selective depression of excitation as measured by the reduction of motility counts effected by the movements of mice during 1 hour after reserpine injection. Levopropranolol is the most potent of the drugs tested, followed by (in descending order of potency) levo-oxprenolol, dextro-propranolol, sotalol, and dextro-oxprenolol. This order of potency does not correspond to the rank order of their

peripheral beta-adrenergic blocking activity. Between the levo-enantiomers and dextro-enantimers, a relation similar to that found in respect to their peripheral beta-adrenergic blocking effects is found: dextro forms are roughly 10 times less potent than the corresponding levo forms. It is suggested that a beta-adrenergic like receptor activity is implicated in the mediation of pargyline and reserpine excitation. Pindolol, which is a strong periphral beta-adrenergic blocking agent, potentiates rather than inhibits the excitation produced by pargyline and reserpine. 29 references. (Author abstract modified)

000090 Domino, E. F. Department of Pharmacology, Lafayette Clinic, Detroit MI 48207 **Search for new treatment approaches in schizophrenia: in vitro studies of potential N-methyltransferase inhibitors.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 221(1):75-86, 1976.

The effects of 129 compounds on partially purified rabbit lung N-methyltransferase (NMT) were studied in order to find potential new therapeutic agents unrelated to current neuroleptic medication in an approach based upon the excess methylation hypothesis of schizophrenia. N-methyltryptamine (NMeT) and 14-C-S-adenosyl-L-Methionine (14C-SAM) were used as substrates in this in vitro procedure to form 14C-N,N-dimethyltryptamine (14C-DMT). S-adenosyl-L-homocysteine (SAH), 2-(2-aminoethyl)-5,6-dichlorobenzimidazole dihydrochloride (SKF 62817-A2), dimethyltryptamine (DMT), an equimolar mixture of adenosine plus DL-homocysteine, N-(2-aminoethyl)-pyrrolidine, and 2-(2-aminoethyl)-pyridine show definite inhibitory properties. It is concluded that further studies, including in vivo determinations of NMT inhibition by these compounds, are indicated. 36 references. (Author abstract modified)

000091 Drawbaugh, R. B.; Lal, H. Department of Pharmacology and Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Effect of pharmacological interference with various neuropathways on blockade of morphine-withdrawal hypothermia by morphine and by conditional stimulus.** Neuropharmacology (Oxford). 15(6):375-378, 1976.

Rats were given two equally spaced injections of morphine sulphate daily, each injection being paired with a bell sound to investigate the hypothermic effects of morphine withdrawal. The morphine dose was gradually increased to 200mg/kg per day. At 24 hr after withdrawal, all rats showed hypothermia which was reversed by either the bell sound or morphine. Morphine alone also produced an overshoot hyperthermia. The bell sound induced alleviation of withdrawal hypothermia was blocked by pretreatment with mecamylamine (2.5mg/kg), phenoxybenzamine (2mg/kg), haloperidol (0.2mg/kg) and benztropine (0.625mg/kg) but was not blocked by cyproheptadine (2mg/kg) or propranolol (2mg/kg). In contrast, morphine induced hyperthermia during withdrawal was blocked by pretreatment with mecamylamine, phenoxybenzamine and cyproheptadine but was not blocked by haloperidol, benztropine, or propranolol. 13 references. (Author abstract)

000092 Drummond, Alan H.; Whigham, Kathryn A. E.; Prentice, Colin R. M. University Department of Medicine, Royal Infirmary, 86 Castle Street, Glasgow G4 OSF, Scotland **Effects of chlorprothixene isomers on platelet 5-hydroxytryptamine receptors: evidence for different 5-hydroxytryptamine conformations at uptake and stimulatory sites.** European Journal of Pharmacology (Amsterdam). 37(2):385-388, 1976.

The effects of the cis and trans-chlorprothixene isomers on platelet 5-hydroxytryptamine (5HT) receptors were studied in humans in an attempt to elucidate stereochemical aspects of the combination of 5HT with its different receptors. The thioxanthene neuroleptic cis-chlorprothixene was approximately 200 times more potent than its transisomer as an inhibitor of the aggregation of human blood platlets induced by 5HT. Against the active uptake of 5HT by these cells, however, trans-chlorprothixene was twice as inhibitory as its cisisomer, and this inhibition was found to be competitive. It is suggested that 5HT adopts different conformations for binding to its two platelet receptors. 10 references. (Author abstract modified)

000093 Dybing, Erik. Dept. of Environmental Toxicology, National Institute of Public Health, Oslo 1, Norway **Inhibition of acetaminophen glucuronidation by oxazepam.** Biochemical Pharmacology (Oxford). 25(12):1415-1425, 1976.

Glucuronidation of 3H-acetaminophen (pHAA) in mouse liver microsomes is enhanced about threefold by 0.025% Triton X-100. Oxazepam inhibits microsomal glucuronidation of pHAA, yielding apparent competitive kinetics in native microsomes. Phenobarbital pretreatment has no effect on the microsomal glucuronidation of pHAA. MH1C1 rat hepatoma cells also glucuronidate pHAA, approximately 40nmoles/mg cell protein per hr being conjugated at a concentration of 1mM. Oxazepam also inhibits pHAA glucuronidation in the cell culture system. Intraperitoneal injection of mice with oxazepam 15 min before subcutaneous injection of pHAA significantly increases the plasma half-life of pHAA. 26 references. (Author abstract)

000094 Elliot, P. N. C.; Huizing, G.; Jenner, P.; Marsden, C. D.; Miller, R. University Department of Neurology, Institute of Psychiatry and King's College Hospital Medical School, Denmark Hill, London SE5 8A, England **Substituted benzamides as dopamine antagonists.** British Journal of Pharmacology (Basingstoke). 57(3):472P, 1976.

Sulpiride, tigan, clebopride and the debenzylated metabolite of clebopride were studied to determine whether their anti emetic and antipsychotic properties are associated with blockade of cerebral dopamine receptors. All of the compounds inhibit apomorphine reversal of reserpine induced akinesia in mice, inhibit the apomorphine induced circling in mice with unilateral 6-hydroxydopamine induced striatal lesions, induce some degree of catalepsy and induce ipsilateral circling in apomorphine treated rats. These compounds induce a rise in the brain concentration of the dopamine metabolite homovanillic acid and, to a lesser extend, the intraneuronal metabolite dihydroxyphenyl acetic acid. Metoclopramide, sulpiride, tigan and the clebopride metabolite have no inhibitory action in the in vitro rat striatal dopamine stimulated adenylate cyclase system. Clebopride causes a small reduction in cyclic AMP production in this system. It is concluded that although these substituted benzamides exert pharmacological and biochemical effects consistent with their being dopamine antagonists, they have little effect in the adenylate cyclase model of the dopamine receptor. Therefore, their mode of action remains an open question. 3 references.

000095 Erwin, V. Gene; Heston, W. D. W.; McClearn, G. E. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins School of Medicine, Baltimore, MD **Effect of hypnotics on mice genetically selected for sensitivity to ethanol.** Pharmacology Biochemistry and Behavior. 4(6):679-683, 1976.

The hypnotic potencies and duration of response of various central nervous system depressants were compared in the long sleep (LS) and short sleep (SS) lines of mice. The data indicate that while the SS and LS lines of mice differ in central nervous system sensitivity to ethanol, methanol, butanol, and t-

butanol it is implied that they do not differ in central nervous system sensitivity to other hypnotic agents tested including sodium pentobarbital, chloral hydrate, trichlorethanol and paradehyde. Proof of this latter suggestion awaits determination of metabolic rates, and brain levels of these other depressants. 18 references. (Author abstract modified)

000096 Filipovic, N.; Stern, P.; Fuks, Z. Institut za Farmakologiju i Toksikologiju Medicinski Fakultet, 71 000 Sarajevo, Yugoslavia **Effects of serine on morphine-dependent mice.** Pharmacology (Basel). 14(3):247-255, 1976.

The possibility that glycine linked mechanisms participate in morphine and morphine antagonist actions was investigated in mice. Administration of 250mg/kg i.p. single doses of serine, the metabolic precursor of glycine, does not elevate central glycine in mice 1 hr after injection or compensate for reduction in central glycine levels caused by implantation of morphine base (70mg/animal). Single doses of serine reduce the jumping response to nalorphine (100mg/kg i.p.). Sustained treatment with 250mg/kg doses of serine at 24 hr intervals produces increases in brain glycine levels and in medullar glycine levels 1 hr after the fourth injection. Glycine levels increase by 39-75% in morphine dependent mice and by 46-50% in controls. The jumping response to nalorphine is enhanced by 40% as compared with controls. Single doses and multiple doses of serine also prevent the development of convulsions after a strongly convulsant dose (0.8mg/kg) of strychnine and markedly reduce strychnine toxicity. It is suggested that serine can mimic the role of glycine in enhancing nalorphine provoked withdrawal behavior in morphine dependent mice and can mimic the antagonism by glycine of some central effects of strychnine. 13 references. (Author abstract modified)

000097 Fisher, Abraham; Grunfeld, Yona; Weinstock, Marta; Gitter, Simon; Cohen, Sasson. Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel **A study of muscarinic receptor heterogeneity with weak antagonists.** European Journal of Pharmacology (Amsterdam). 38(1):131-139, 1976.

Heterogeneity among muscarinic receptors was studied with new rigid molecules, comprising structures in the fused quinuclidine valerolactone, quinuclidine cyclohexenone, quinuclidine cyclohexanone and quinuclidine cyclohexane derivatives. These are structurally related to the potent muscarine agent, 3-acetoxyquinuclidine, but substantially different from its conformation. All proved to antagonize acetylcholine like activity, but to a different extent in different systems. The equipotent molar rate with respect to atropine (as 1) was: isolated guinea-pig ileum 10,000 to 1000; mouse salivary gland 1000 to 100; cat superior cervical ganglion 100 to10; and mouse central nervous system approximately 10. It is suggested that the rigid structure induces a three point constrained fit in the receptor (onium group, hydrophobic moiety and carbonyl group), but that not all muscarinic receptors are capable of responding equally. In this case, receptor specificity of the drug is a direct consequence of its graded departure from the perferred conformation of acetylcholine and, therefore, is necessarily associated with partial loss of potency. 20 references. (Author abstract)

000098 Forbes, James E.; Dewey, William L. Dept. of Pharmacology, Medical College of Virginia, Virginia Commonwealth Univ., Richmond, VA 23298 **The effects of narcotic analgesics and narcotic antagonists on ganglionic transmission in the rat.** Life Sciences (Oxford). 19(3):401-407, 1976.

The effects of narcotic analgesics, narcotic antagonist analgesics, and narcotic antagonists on ganglionic transmission in the superior cervical ganglia of the rat were studied in vivo and in vitro. In vivo administration of morphine, meperidine, methadone, pentazocine or naltrexone blocked ganglionic transmission. Levorphanol, cyclazocine, nalorphine, and naloxone had no effect on ganglionic transmission in vivo. But, levorphanol, cyclazocine, nalorphine, phorphine, mereridine, methadone, pentazocine, and naltrexone blocked ganglionic transmission in vitro. In both preparations, naloxone did not antagonize the effect of morphine, suggesting that the effects of morphine and the other opiates were nonspecific. Similar potency of d-isomers and l-isomers of pentazocine and cyclazocine support this conclusion. The observation that naltrexone blocked ganglionic transmission, but the other pure narcotic antagonist, naloxone, was inactive is somewhat unique to this test procedure and possibly significant. 18 references. (Author abstract modified)

000099 Fratta, Walter; Mereu, Giampaolo; Chessa, Paolo; Paglietti Elisabetta; Gessa, GianLuigi. Institute of Pharmacology, University of Cagliari, Cagliari, Italy. **Benzodiazepine-induced voraciousness in cats and inhibition of amphetamine-anorexia.** Life Sciences (Oxford). 18(10):1157-1165, 1976.

The effect of different benzodiazepines on food intake was studied in cats trained to eat their daily food within 3 hours, under conditions in which emotional inhibitory factors were not present. The order of decreasing potency of benzodiazepines tested was: oxazepam, N-methyl-lorazepam diazepam, chlordiazepoxide, pinazepam, medazepam. When they were administered (at a dose ranging from 0.1to 3mg/kg) before feeding, they increased both total amount of food eaten and also rate at which food was ingested. When administred at the end of feeding period, these compounds made the animals resume eating voraciously. Oxazepam (3mg/Kg) stimulated food intake maximally, even when administered up to 12 hours before feeding. Finally, oxazepam antagonized the anorexigenic effect of d-amphetamine, but did not influence amphetamine induced hyperactivity and stereotyped behavior. 17 references. (Author abstract modified)

000100 Fredholm, Bertil B.; Fuxe, Kjell; Agnati, Luigi. Department of Human Physiology, University of Bologna, Bologna, Italy **Effect of some phosphodiesterase inhibitors on central dopamine mechanisms.** European Journal of Pharmacology (Amsterdam). 38(1):31-38, 1976.

The effect of five phosphodiesterase (PDE) inhibitors (including papaverine) was studied on adenylate cyclase and on cyclic nucleotide PDE activities in extracts of rat caudate nucleus, and compared to the effect on dopamine (DA) turnover and on turning behavior in rats with unilateral lesions of the nigro-neostriatal DA neurons. The data are compatible with the opinion that PDE inhibition leads to be an enhanced effect of DA in the caudate nucleus. However, the results also demonstrate that several of the PDE inhibitors have effects on central DA mechanisms that are difficult to explain solely on the basis of PDE inhibition. 22 references. (Author abstract modified)

000101 Fuller, Ray W.; Snoddy, Harold D.; Molloy, Bryan B. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Pharmacologic evidence for a serotonin neural pathway involved in hypothalamus-pituitary-adrenal function in rats.** Life Sciences (Oxford). 19(3):337-345, 1976.

Male Wistar derived albino rats were injected with fluoxetine hydrochloride and 5-hydroxytryptophan (5HTP) in a search for evidence of serotonin neural pathways involved in hypothalamus pituitary adrenal function in rats. Fluoxetine, an

inhibitor of serotonin reuptake, caused a dose related elevation of plasma corticosterone levels in intact but not in hypophysectomized rats. The elevation of plasma corticosterone by 5HTP was shown to be stereospecific with L-5HTP being much more active than D-5HTP. Simultaneous injection of subeffective doses of fluoxetine and L-5HTP caused marked elevations of plasma corticosterone. Fluoxetine pretreatment potentiated the elevation of plasma corticosterone by L-5HTP. The data support the existence of a previously postulated serotoninergic neural pathway stimulating adrenocorticotropin release in rats. 18 references. (Author abstract modified)

000102 Furukawa, T.; Sano, T.; Kohno, Y.; Koga, M.; Nagasaki, N. Department of Pharmacology, School of Medicine, Fukuoka University, Fukuoka 814, Japan **Selective depleting effect of syrosingopine on brain catecholamine levels with relation to morphine analgesia in the rat.** Pharmacology, Biochemistry and Behavior. 4(4):419-425, 1976.

Reserpine was the most potent, rescinnamine the next and syrosingopine -- a synthetic analogue of reserpine -- the weakest in the depleting effects on brain amines of rauwolfia alkaloids. After syrosingopine, brain dopamine (DA) was decreased to a smaller degree and with a shorter duration as compared with norepinephrine (NE) and serotonin (5-HT), whereas reserpine elicited a marked and long lasting reduction in these amines. Accordingly, syrosingopine induced a depletion of brain NE and 5-HT without alteration in brain DA content 2-4 days after administration. Repeated administrations of syrosingopine for 2 or 4 days, resulted in similar alterations in brain amine levels. This selective depleting effect of syrosingopine on brain amines was potentiated by combined treatment with disulfiram or fusaric acid, a dopamine beta-hydroxylase inhibitor. Under the condition of selective depletion of brain amines induced by repeated administrations of syrosingopine the analgesic action of morphine was not affected, whereas reserpine and tetrabenazine antagonized morphine analgesia, concomitant with inducing a depletion of all brain amines. Results suggest that brain DA may be more important than brain NE or 5-HT with regard to the mechanisms by which morphine produces analgesia. 39 references. (Author abstract modified)

000103 Gage, Fred H.; Olton, David S. Department of Psychology, Johns Hopkins University, Baltimore, MD 21218 **L-dopa reduces hyperreactivity induced by septal lesions in rats.** Behavioral Biology. 17(2):213-218, 1976.

The hypothesis that hyperreactivity observed after septal lesions may be partly caused by a depletion of brain catecholamines and that its gradual disappearance may be caused by the recovery of normal brain catecholamine levels was tested in albino rats. Rats with septal lesions exhibited a significant increase in reactivity. Administration of a single dose of either 50, 100, 225, 300, 400, or 475mg/kg of L-dopa and R04-4602 (a peripheral decarboxylase inhibitor) resulted in a dose related increased rate of disappearance of the hyperreactivity induced by septal lesions. Injection of an equal volume of vehicle did not produce any noticable effect. Findings supported the hypothesis. 14 references. (Author abstract modified)

000104 Gale, Karen N.; Guidotti, A. NIMH, St. Elizabeths Hospital, Washington, DC 20032 **GABA-mediated control of rat neo-striatal tyrosine hydroxylase revealed by use of intranigral muscimol.** Bethesda, MD, NIMH, 1976. 12 p.

The hypothesis of gamma-aminobutyric acid (GABA) control of rat neostriatal tyrosine hydroxylase was tested using intranigral muscimol, an isoxazol derivative with a restricted conformation similar to that of GABA which displays bicuculline sensitive and strychnine insensitive inhibitory activity both in vivo and in vitro. Findings demonstrate the possibility of interfering with haloperidol induced activation of caudate-putamine (CP)/tyrosine hydroxylase (TH) by pharmacologically maintaining the functional effect of GABA on nigral neurons. Findings suggest that the musicimol/haloperidol interaction occurred directly in the nigra. Thus, the release of dopamine (DA) by nigral dendrites and a postulated self-inhibitory action of DA in substantia nigra may not be relevant to the mechanism of neuroleptic activation of CP/TH. Instead, it seems that haloperidol acts to change activity in nigral neurons indirectly as a result of its action in neostriatum. Application of muscimol directly into nigra, by mimicking GABA, probably acted to preclude the influence of a striato/nigral feedback pathway. This implies that a decrease in GABA release in nigra is required for the neuroleptic induced activation of CP/TH, muscimol blockade. 22 references.

000105 Garey, Richard E.; Heath, Robert G. Dept. of Psychiatry and Neurology, Tulane University School of Medicine, New Orleans, LA 70112 **The effects of phencyclidine on the uptake of 3H-catecholamines by rat striatal and hypothalamic synaptosomes.** Life Sciences (Oxford). 18(10):1105-1110, 1976.

In tests of the effects of the psychotomimetic agent, phencyclidine 1-(1-phenylcyclohexyl) piperidine (PCP), on the uptake of 3H-catecholamines by synaptosome rich homogenates of rat striatum and hypothalmus, PCP was shown to be a potent, competitive inhibitor of both 3H-dopamine in the striatal region and 3H-norepinephrine uptake in the hypothalamus. Implications of these findings are discussed as a drug induced imbalance of the catecholaminergic/cholinergic systems in those regions of the brain where activity has been correlated with emotional expression. The unique psychopharmacological properties of PCP described here tend to support the model which postulates that acute psychotic states are the result of an imbalance between dopaminergic and cholinergic systems in brain regions involved in emotional expression. 22 references. (Author abstract modified)

000106 Geber, W. F.; Lefkowitz, S. S.; Hung, C. Y. Department of Pharmacology, Medical College of Georgia, Augusta, GA 30902 **Action of Naloxone on the interferon-lowering activity of morphine in the mouse.** Pharmacology (Basel). 14(4):322-329, 1976.

The serum titer of interferon produced by polyinosinic: polycytidylic acid (polyI:C) was studied. Both morphine and naloxone produced a significant decrease in the ability of mice to increase the serum titer of interferon in response to poly I:C. Naloxone appeared to function as an antagonist to morphine when administered following morphine injection, results were interpreted to indicate the possibility that naloxone could function as both an antagonist and agonist under this condidtion. 32 references. (Author abstract modified)

000107 George, A. J. Pharmacology Department, School of Pharmacy, Liverpool Polytechnic, Liverpool, England **The effects of three tricyclic antidepressants on arterial 3HNA uptake and arterial responsiveness to noradrenaline (NA).** British Journal of Pharmacology (Basingstoke). 57(3):432P-433P, 1976.

The effects of imipramine, amitriptyline and clomipramine on arterial noradrenaline uptake and arterial responsiveness to

noradrenaline were investigated in vitro, using rat mesenteric arteries. Each drug causes a potentiation of the responses to noradrenaline above the control values. Each drug also inhibits uptake of noradrenaline when compared to control values. At a concentration of 1x10 to the minus 8M, clomipramine inhibits noradrenaline uptake by 30%, amitriptyline inhibits uptake by 15% and imipramine inhibits uptake by 20%. At a concentration of 1x10 to the minus 6M, noradrenaline uptake is inhibited by 80%, 65% and 55% by imipramine, amitriptyline, and clomipramine respectively. There is a direct correlation between the effects of each drug on noradrenaline uptake and the effects on arterial responsiveness to noradrenaline. It is suggested that the difference in potency between clomipramine and the other compounds at different perfusion concentrations might explain the greater effectiveness of clomipramine in some disorders such as obsessional neurosis. 5 references.

000108 Gershon, Michael D.; Brooks, Dana C. 630 W. 168 St., Columbia University College of Physicians and Surgeons, New York, NY 10032 **Monoamine oxidase inhibition and the induction of ponto-geniculo-occipital wave activity by reserpine in the cat.** Journal of Pharmacology and Experimental Therapeutics. 197(3):556-566, 1976.

An investigation was carried out to determine: 1) the relationship between monoamine oxidase (MAO) inhibition and the ponto-geniculo-occipital (PGO) wave activity produced by reserpine administration; 2) whether MAO inhibition affects PGO activity during wakefulness or PGO activity during rapid eye movement (REM) sleep; 3) whether actions on PGO waves during REM sleep can be separated from suppression of REM itself; 4) whether suppression of PGO waves can be related to the concentration of serotonin in the brain; and 5) whether the specific intraneuronal A-type MAO or the nonspecific B-type MAO is related to suppression of PGO waves. Reserpine induces PGO wave activity in the cat similar to that seen during the REM phase of sleep. This action of reserpine was blocked by the MAO inhibitors, pheniprazine, harmaline and clorgyline, but not by deprenyl or its demethylated analog. After a single dose (20mg/kg) of either pheniprazine or harmaline, the time course of antagonism of the effect of reserpine was in good correspondence with inhibition of MAO but not with restoration of the serotonin content of several regions of the brain. Harmaline had a reversible effect while that of pheniprazine persisted for weeks. Clorgyline in low doses (0.5-1.0mg/kg), at which it is a specific inhibitor of A-type MAO, antagonized the action of reserpine for over 2 weeks. Deprenyl and its demethylated analog failed to suppress the reserpine induced waves even at 10 times the dose of clorgyline when they should have completely inhibited B-type MAO. In contrast to antagonism of reserpine, suppression of REM sleep by these MAO inhibitors could be temporally dissociated from their inhibition of the enzyme. It is concluded that suppression of the induction of PGO waves by reserpine after administration of the MAO inhibitors is a specific effect of these drugs and is related to inhibition of A-type MAO. Suppression of REM sleep is probably a nonspecific effect and not related to inhibition of the enzyme. 42 references. (Author abstract modified)

000109 Ghosh, M. N.; Parvathy, S. Department of Pharmacology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry-6, India **Tolerance pattern of the anorexigenic action of amphetamines, fenfluramine, phenmetrazine and diethylpropion in rats.** British Journal of Pharmacology (London). 57(4):479-485, 1976.

The tolerance pattern to anorectic drugs (amphetamines, fenfluramine, phenmetrazine and diethylpropion) was studied in starved rats by measuring two consecutive 2 hr food intakes. There was a reduction in the first 2 hr food intake with development of complete tolerance after fenfluramine and phenmetrazine, and of partial tolerance after amphetamine, (plus)-amphetamine and diethylpropion. During the second 2 hr intake, the anorectic effect was transient after fenfluramine and diethylpropion; while there was an absolute increase in the intake after amphetamine and (plus)-amphetamine. The results indicate that so called tolerance to the anorexigenic effect of drugs is apparent rather than real and the duration of food access is a termining factor. The body weight changes may be brought about by the metabolic effects of these drugs rather than their effect on food and water intake. 13 references. (Author abstract modified)

000110 Gibbs, Marie E.; Barnett, J. M. Department of Psychology, La Trobe University, Bundoora 3083, Australia **Drug effects on successive discrimination learning in young chickens.** Brain Research Bulletin. 1(3):295-299, 1976.

Chicks were trained to avoid pecking either a red or a blue bead in a one trial avoidance task by coating one bead with methyl anthranilate. Intracranial administration of ouabain or cycloheximide (CXM) resulted in decay in retention after 10 and 30 min respectively. In a second experiment, chicks were trained on three physically distinct beads, two of which were made aversive during the learning period. Saline, ouabain, or CXM were administered immediately before training on one or another test bead. Saline tested chickens retained memory of both aversive beads on retention trials. CXM and ouabain treated chickens showed loss of memory for the bead associated with the drug with which they were treated but showed retention of the task which was not associated with the drug. 6 references. (Author abstract modified)

000111 Gilman, Sara C.; Fischer, Gloria J. Department of Pharamcology, Naval Research Institute, Bethesda, MD 20014 **The effects of diethyldithiocarbamate on passive avoidance learning by chicks (Gallus domesticus).** Psychopharmacology (Berlin). 48(3):287-289, 1976.

The possible relationship between norepinephrine (NE), neural systems, and passive avoidance learning was investigated in chickens. Diethyldithiocarbamate (DDC), a competitive inhibitor of dopamine beta-hydroxylase, produced a dose related depletion of neural NE and impairment of passive avoidance learning. Retention of the learned task was not impaired. It is suggested that neural NE depletion impairs ability to inhibit responding and therefore indirectly impairs passive avoidance learning or inhibitory avoidance learning. Alternatively, NE depletion may slow learning by interfering with consolidation. 13 references. (Author abstract modified)

000112 Gispen, W. H.; Reith, M. E. A.; Schotman, P.; Wiegant, V. M.; Zwiers, H.; Bohus, B.; De Wied, D. University of Utrecht, Utrecht, The Netherlands **Neuropeptides, brain and behavior.** Research in Neurosis. Bohn, Scheltema and Holkema, 1976. (p. 192-202).

The effect and mechanism of action of the pituitary peptide ACTH in brain and behavior is discussed, and electrophysiological and neurochemical research revealed a direct stimulatory effect of ACTH like peptides on nerve tissue. Delay of extinction of a previously learned response may be regarded as a rather inadequate behavior, and it is therefore that the hypothesis is put forward that disregulation or chronic activation of pituitary activity may contribute to the develop-

ment and maintenance of psychoneurosis through the abnormal discharge of neuropeptides. 7 references. (Author abstract modified)

000113 Gorecki, Dennis K. J.; Peesker, Sylvester J.; Wood, James D. Department of Biochemistry, University of Saskatchewan, Saskatoon, Canada **3-Isoxazolidone -- an inhibitor of GABA metabolism.** Biochemical Pharmacology (Oxford). 25(14):1653-1657, 1976.

In order to circumvent the impermeability of the blood-brain barrier to aminooxypropionic acid, the cyclic analogue 3-isoxazolidone was prepared and administered intramuscularly to animals, and its effects on brain glutamic acid decarboxylase (GAD) and gamma-aminobutyric acid (GABA) were studied. Systemic administration of 3-isoxazolidone results in potent inhibitions of brain GAD and GABA-alpha-oxoglutarate aminotransferase (GABA-T) activities. A small but significant increase in brain GABA content occurs. The inhibiting effects vary with the experimental species, being greatest in chicks and least in mice. The enzyme inhibitions are not prevented by the concurrent administration of pyridoxine to the animals nor by the addition of pyridoxal phosphate to the assay system. Additions of 3-isoxazolidone directly to brain homogenates inhibits the activities of both GAD and GABA-T, but not to the extent that might be expected from the in vivo studies. It is suggested that 3-isoxazolidone, or a metabolite, penetrates the blood-brain barrier. Whether these inhibitions are due to the action of the drug or by aminooxypropionic acid formed in vivo is not clear. Although 3-isoxazolidone may prove useful as a tool with which to study GAD and GABA-T enzyme systems, its potent inhibition of GAD activity with the attendant danger of seizures precludes any role for the compound as a possible therapeutic agent. 26 references. (Author abstract modified)

000114 Greer, Charles A.; Alpern, Herbert P.; Collins, A. C. Dept. of Psychology, University of Colorado, Boulder, CO 80309 **Increased CNS sensitivity to flurothyl as a measure of physical dependence in mice following morphine, phenobarbital, and ethanol treatment.** Life Sciences (Oxford). 18(12):1375-1382, 1976.

To test the CNS sensitivity to flurothyl as a measure of physical dependence, male C57BL/6 mice were administered either morphine, phenobarbital, or ethanol in their drinking water in order to induce dependency. During withdrawal, onset of myoclonus,, clonus and tonus was evaluated with flurothyl, a convulsant inhalant. Morphine, phenobarbital, and ethanol treated subjects displayed significantly lower latencies for myoclonic and clonic convulsive behavior when compared with their respective controls. The increased CNS excitability observed is characteristic of physical dependence, and the flurothyl technique employed is discussed in light of its broad applicability to a number of agents characterized by their dependence producing properties. 17 references. (Author abstract modified)

000115 Griffiths, R; Tudball, N. Department of Biochemistry, University College, Cathays Park, P.O. Box 78, Cardiff CF1 1XL, Wales **Observations on the fate of cystathionine in rat brain.** Life Sciences (Oxford). 19(8):1217-1224, 1976.

Direct intracerebral administration of 35S-cystathionine has been shown to be capable of labeling the normal pools of cystathionine in rat brain tissue and thus capable of yielding useful information about the metabolic fate of the amino acid. Cystathionine was shown to be metabolized slowly to yield inorganic sulphate, taurine, and cystine. Subcellular fractionation studies concerned with the distribution of 35S-cystathionine coupled with similar investigations involving enzymes of the transsulfuration pathway indicate that cystathionine fulfills some of the requirements of a neurotransmitter substance. 20 references. (Journal abstract)

000116 Grupp, L. A.; Linseman, Mary Ann; Cappell, Howard. Addiction Research Foundation, Toronto, Ontario M5S 2S1, Canada **Effects of amygdala lesions on taste aversions produced by amphetamine and LiCl.** Pharmacology Biochemistry and Behavior. 4(5):541-544, 1976.

An investigation was carried out to determine whether the attenuation in the lithium chloride induced taste aversion brought about by lesions to the amygdala reported by Nachman and Ashe (1974) would also occur when an unconditioned stimulus (UCS) with different systemic effects was used. Rats which sustained bilateral damage to the amygdala were treated with dextroamphetamine sulfate (4mg/kg) or with lithium chloride (12.5mg/kg of a 0.24M solution). An attenuation of the taste aversion occurs in both amphetamine treated animals and in lithium chloride treated animals. It is concluded that the effect of lesions of the amygdala on taste aversion is not UCS specific. The hypothesis of Nachman and Ashe concerning the role of the amygdala in taste aversion conditioning is supported by the indication that regardless of the particular effects any one UCS may have, the ability of the substance to produce a taste aversion is partially dependent on the normal functioning of the amygdala. 10 references.

000117 Gullis, R. J.; Rowe, C. E. Max-Planck-Institut fur Biochimie, 8033 Martinsried bei Munchen, Germany **Pharmacological studies on the stimulation of the phospholipase A2-acylation system of synaptic membranes of brain, by neurotransmitters and other agonists.** Journal of Neurochemistry (Oxford). 26(6):1217-1230, 1976.

The effects of antagonists known to be specific in other tissue systems on stimulation of the phospholipase A2-acylation system of synaptic brain membranes were examined in guinea pig cerebral cortex. Results indicated that: 1) methacholine, nicotine, and succinylcholine stimulated the system, while stimulation by acetylcholine was partially blocked by atropine and by D-tuberocurarine respectively; 2) the system was stimulated by phenylephrine and isoproterenol, while that by noradrenaline was partially blocked by phenoxybenzamine and pindalol respectively; 3) stimulation of both acylation and phospholipid hydrolysis by 5-hydroxytryptamine and histamine were partially blocked by methysergide and diphenydramine; 4) high concentrations of dichloroisoproterenol, atropine, methysergide, diphenhydramine, strychnine, picrotoxin, and eserine stimulated the system; 5) synergistic stimulations of both acylation and hydrolysis of phosphatidylcholine were observed by adenosine combined with noradrenaline, 5-hydroxytryptamine, histamine, dopamine, or gamma-aminobutyric acid, respectively; 6) in the presence of ATP-McC12, synergistic stimulations of the hydrolysis of phosphatidylcholine were observed after 30 s by noradrenaline combined with 5-hydroxytryptamine, histamine, dopamine, gamma-aminobutyric acid or carbamoylcholine, respectively. Results are discussed with reference to the known ability of agonists to form cyclic nucleotides. 32 references. (Author abstract modified)

000118 Haacke, H.; Johnsen, K.; Kolenda, K.-D. II. Medizinische Univ.-Klinik Kiel, Metzstr. 53/57, D-2300 Kiel, W. Germany **Interaction of pentobarbital, diphenylhydantoin and digitoxin with ethanol in the isolated perfused guinea-pig liver.** Arzneimittel-Forschung (Aulendorf). 26(5):835-839, 1976.

The effects of ethanol on the metabolism of 14C-pentobarbital, 14C-diphenylhydantoin and 3H-digitoxin were investigated in vitro using isolated guinea-pig liver. The disappearance of ethanol from the perfusion medium can be described by zero order kinetics and is not affected by the three drugs. After a short period of distribution, the disappearance of pentobarbital and diphenylhydantoin from the perfusion medium is speeded in the presence of ethanol, and uptake of these drugs into liver tissue is increased. The drugs accumulate in the liver primarily unchanged, suggesting that the inhibition of drug metabolism by ethanol is the cause of the altered distribution. Ethanol does not significantly alter the distribution or the pronounced biliary excretion of digitoxin. However, some evidence exists that ethanol inhibits the metabolism of digitoxin to some extent. It is suggested that the combination of ethanol and drugs can produce a metabolic interference resulting in changes in the pharmacokinetics and altered distribution of the drugs. Inhibition of metabolism can therefore result in lowering the blood level if distribution in the organs is altered simultaneously. 34 references.

000119 Hahn, Dong Soo; Lee, Chung Kyoon. Department of Psychiatry, School of Medicine, Seoul National University, Seoul, Korea **Lithium carbonate distribution and its effects on the other ions in the brain and the other tissues of rats.** Neuropsychiatry (Seoul). 14(4):460-470,1975.

The distribution of lithium and the effects of lithuim administration on levels of sodium (Na), potassium (K), calcium (Ca), and magnesium (Mg) in the brain and other tissues were studied in control animals, in rats receiving prolonged administration of low doses of lithium, and in rats receiving larger doses of lithium for a short period of time. The presence of small amounts of lithium in control animals is demonstrated. Lithium infiltrates rapidly into the liver, skin, and kidney; less rapidly into the muscles and bones; and slowly into the brain and the red blood cells. Infiltration is most rapid and higher tissue levels of lithium are achieved in the brain and most organs (except the hypophysis and the adrenal glands) after administration of larger doses. Lithium decreases Na and K in the brain and increases K in muscle; Ca and Mg concentrations in the brain are unaffected. Lithium increases Ca in muscle, heart, liver, and kidney, and increases Mg in plasma, kidney, and red blood cells. High doses of lithium increase plasma levels of Ca but small doses decrease plasma Ca levels slightly. 49 references.

000120 Hamon, M.; Bourgoin, S.; Enjalbert, A.; Bockaert, J.; Hery, F.; Ternaux, J. P.; Glowinski, J. Laboratoire de neurophysiologie, College de France, 11, place Marcelin Berthelot, F-75231 Paris Cedex 5, France **The effects of quipazine on 5-HT metabolism in the rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(1):99-108, 1976.

Since quipazine is a potent serotonin (5-HT) agonist in peripheral organs, its possible stimulatory effects on serotoninergic receptors in the rat brain were investigated. Quipazine administration induced a significant decrease in the synthesis and turnover rates of serotonin in the brain stem as well as in the forebrain. It is not likely that these changes were mediated by a negative feedback mechanism triggered by a direct action of quipazine on central 5-HT postsynaptic receptors. In contrast to LSD and 5-methoxy-N,N-dimethyltryptamine, this compound failed to activate the 5-HT sensitive adenylate cyclase in colliculi homogenates of newborn rats. However, quipazine exerted direct effects on serotoninergic terminals. It inhibited competitively the reuptake process in synaptosomes and stimulated the K plus evoked release of newly synthesized 3H-5-HT in slices of the brain stem. Injected in vivo in a dose which affected 5-HT uptake and release, quipazine did not modify MAO activity. However, this activity was noncompetitively inhibited by high concentration of the drug in vitro. These actions are very likely indirectly responsible for the stimulation of central 5-HT receptors. 33 references. (Author abstract modified)

000121 Himori, Norio; Taira, Norio. Department of Pharmacology, Tohoku University School of Medicine, Sendai 980, Japan **Release of noradrenaline proposed as a mechanism for the positive inotropic action of dipyridamole.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(1):31-37, 1976.

In the arterially blood perfused canine papillary muscle, i.a. injections of dipyridamole (10-300 micrograms) produced a dose dependent increase in developed tension at 300 micrograms. The positive inotropic response to dipyridamole was greatly reduced by a prior i.a. injection of propranolol or by pretreatment with reserpine but not affected by a prior i.a. injection of tetrodotoxin or desmethylimipramine. The positive inotropic response to dipyridamole reduced by pretreatment with reserpine was restored by i.a. infusion of noradrenaline. Dipyridamole did not modify the positive inotropic responses to noradrenaline and tyramine. These results suggest that the positive inotropic response to dipyridamole is largely due to noradrenaline released from adrenergic nerve endings by a mechanism that differs from those operative in the action of tyramine or in the liberation of noradrenaline upon excitation. 20 references. (Author abstract modified)

000122 Ho, I. K.; Yamamoto, I.; Becker, K. E.; Loh, H. H.; Way, E. L. University of Mississippi Medical Center, Jackson, MS 39216 **Enhancement of pentobarbital effect by continuous administration of morphine in the mouse.** Life Sciences (Oxford). 19(3):357-365, 1976.

The effect of chronic morphine administration on pentobarbital induced narcosis and hypothermia, and possible biochemical mechanisms underlying this effect, were investigated in mice. The data demonstrate markedly increased brain and serum levels and brain/serum ratios of pentobarbital after continuous but not after single acute administration of morphine. The data demonstrate that continuous treatment with morphine increased pentobarbital induced narcosis and hypothermia. They also show that an increase in pentobarbital response was related to inhibition of N-demethylase activity in the liver which was used as an indirect measurement of hepatic drug metabolizing enzyme activity. The increased brain uptake of pentobarbital in morphine treated animals may also contribute to the enhancement of pentobarbital response. 26 references.

000123 Hoffman, W. E.; Phillips, M. Ian. Neurobehavior Laboratory, Department of Physiology and Biophysics, University of Iowa, Iowa City, IA 52242 **Regional study of cerebral ventricle sensitive sites to angiotensin II.** Brain Research (Amsterdam). 110(2):313-330, 1976.

The site of action for both the increase in blood pressure and the short latency drinking behavior produced by injection of small doses of angiotensin II was studied in rats. The response to several doses of angiotensin delivered to each ventricle was investigated with multiple ventricular cannulation. This revealed that the rostral ventricular system is involved in angiotensin II mediated responses. Limiting cerebrospinal fluid flow by plugging specific anterior ventricular regions and

posterior ventricular regions revealed that the ventral anterior third ventricle must be reached by the peptide in order to produce blood pressure elevation or drinking behavior effects. In order to separate pressor components due to vasopressin release and sympathetic activation, hypophysectomized rats were also tested. The pressor response to intraventricular angiotensin II is due to both sympathetic hormonal components and pituitary hormonal components and both are dependent on sites sensitive to angiotensin in the anterior third ventricle. It is suggested that the ventral anterior third ventricle or the periventricular tissue surrounding it is essential for both blood pressure responses and drinking responses to intraventricular angiotensin II. 22 references. (Author abstract modified)

000124 Holroyde, Martin C.; Eyre, Peter. Pharmacology Laboratory, Dept. of Biomedical Sciences, University of Guelph, Guelph, Ontario, Canada **Inhibition by 5-hydroxytryptamine or anaphylactic histamine release from bovine granulocytes.** European Journal of Pharmacology (Amsterdam). 37(2):397-399, 1976.

A pure granulocyte fraction was isolated from the venous blood of four calves previously sensitized to horse plasma, and aliquots of this fraction were tested to determine the inhibition of anaphylactic histamine release by 5-hydroxytryptamine (5HT). Histamine release was strongly inhibited by 5HT in a dose related fashion. It is thought that this is a first report of any response to 5HT in an immunological system such as this. It is suggested that it is important in view of the proven release of 5HT from sensitised bovine lung, and its probable contribution to the development of the varied symptoms of systemic anaphylaxis in this species. 16 references. (Author abstract modified)

000125 Horn, Alan S.; Phillipson, Oliver T. M.R.C. Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, University of Cambridge, Cambridge, England **A noradrenaline sensitive adenylate cyclase in the rat limbic forebrain: preparation, properties and the effects of agonists, adrenolytics and neuroleptic drugs.** European Journal of Pharmacology (Amsterdam). 37(1):1-12, 1976.

A method for the preparation of a noradrenaline sensitive adenylate cyclase from homogenates of the rat limbic forebrain using Krebs-Ringer as the homogenizing medium is described. Response of the enzyme to agonists are characteristic of a beta1-receptor in that the potency of l-isoprenaline (l-isoproterenaol) exceeds that of l-noradrenaline (l-NA) which exceeds that of l-adrenaline. A strict requirement for a catechol moiety and a beta-hydroxyl group in the structure of the agonist is indicated by the fact that dopamine, d,l-octopamine, d,l-normetanephrine and l-metaraminol are all inactive. Stimulation of cyclic AMP production by noradrenaline and adrenaline is stereoselective while with isoprenaline, the stimulation is stereospecific. The activation of the enzyme by l-NA is sensitive to stereoselective inhibition by l-propranolol. Examination of a number of neuroleptic drugs, including promazine, clozapine, thioridazine, trifluperazine, alphaflupenthixol, pinozide, and butaclamol, showed promazine to be the most effective agent tested in antagonizing the stimulation produced by l-noradrenaline. Alpha-flupenthixol is only weakly active and the antagonism produced by the alpha isomer and the beta isomer of the drug is not stereoselective. Pimozide is not a potent antagonist. The spectrum of antagonism produced by neuroleptic drugs is quite different from that seen in the dopamine sensitive adenylate cyclase of the rat corpus striatum. It is suggested that the antipsychotic effects of the potent neuroleptics are probably predominantly mediated through an interaction with dopamine sensi tive receptors rather than noradrenaline sensitive receptors in the brain. 42 references. (Author abstract modified)

000126 Hotujac, L.J.; Muftic, R.H.; Filipovic, N. Department of Pharmacology, PLIVA, Pharmaceutical and chemical Works, J. L. Rivara 89, 41001 Zagreb, Yugoslavia **Verruculogen: a new substance for decreasing of GABA levels in CNS.** Pharmacology (Basel). 14(4):297-300, 1976.

THe mechanism of action of verruculogen induced tremors by decreasing GABA levels in the CNS is examined in the mouse brain. Verruculogen is a new tremorogenic substance isolated from the mold of Penicillium verruculosum Peyronel. Results indicate that verruculogen tremor is mediated by a loss of inhibitory GABA function. Verruculogen induced tremor was accompanied by a significant reduction in GABA levels. It is concluded that verruculogen may be a useful tool for further defining the inhibitory role of GABA in CNS function. 15 references.

000127 Houser, Vincent P. RD No 1, Box B95, Route 94, Chester, NY 10918 **Modulation of the aversive qualities of shock through a central inhibitory cholinergic system in the rat.** Pharmacology Biochemistry and Behavior. 4(5)561-568, 1976.

The effects of central acting cholinergic stimulants, central acting anticholinergics, peripheral acting cholinergic stimulants and peripheral acting anticholinergics in modifying the aversive qualities of electric shock were studied in naive rats. Central cholinergic stimulation via the administration of pilocarpine or arecoline elevates the threshold for grid shock, while the central acting anticholinergics scopolamine and atropine produce decrements in the threshold. Peripheral acting anticholinergics (methylscopolamine and methylatropine) are less potent than central acting drugs given in equivalent doses, while peripheral cholinergic stimulants (neostigmine and carbachol) are inactive. Pilocarpine, but not carbachol, blocks the decrements noted in response to scopolamine hydrobromide administration. Arecoline, but not nicotine, elevates the aversive threshold. It is suggested that muscarinic receptor sites are probably involved in mediating the effects of central cholinergic stimulants. 12 references. (Author abstract modified)

000128 Iwamoto, Edgar T.; Loh, H. H.; Way, E. Leong. University of California, San Francisco, CA 94143 **Dopaminergic-cholinergic interactions in naloxone-induced circling in morphine-dependent rats with nigral lesions.** European Journal of Pharmacology (Amsterdam). 38(1):39-54, 1976.

The effect of dopaminergic and cholinergic agonists and antagonists on naloxone precipitated contralateral circling and withdrawal behavior in morphine dependent rats with unilateral lesions of the substantia nigra zone compacta was investigated. Following challenge with a supramaximal naloxone dose, both continuous and contralateral circling behavior and severe withdrawal signs in morphine dependent, lesioned rats were elicited. After various drug pretreatments, the contralateral circling behavior precipitated by naloxone was: 1) reversed to ipsilateral circling by intraperitoneal apomorphine or d-amphetamine; 2) unaltered by intraperitoneal haloperidol or intraneostriatal arecoline administered into the intact neostriatrum; and 3) reversed to ipsilateral circling by the administration of atropine into the intact neostriatum. Atropine, apomorphine and amphetamine all interfered with the manifestation of naloxone precipitated abstinence. These data suggest that a diminution of dopaminergic or an enhancement of cholinergic activities, or both, occur at the level of the neos-

triatum during naloxone precipitated withdrawal in morphine dependent rats. 42 references. (Author abstract modified)

000129 Jackson, D, M.; Malor, R.; Chesher, G. B.; Starmer, G. A.; Welburn, P. J.; Bailey, Ruth. Department of Pharmacology, University of Sydney, N.S.W., 2006, Australia **The interaction between prostaglandin E1 and delta9-tetrahydrocannabinol on intestinal motility and on the abdominal constriction response in the mouse.** Psychopharmacology (Berlin). 47(2):187-193, 1976.

The interaction between delta9-tetrahydrocannabinol (THC) and prostaglandin E1 (PGE1) was studied using two pharmacological parameters: the rate of passage of a charcoal meal through mouse small intestine, and the abdominal constriction response in the mouse. PGE1 administered intraperitoneally produced a dose dependent decrease in intestinal motility, and this effect was antagonized by low doses of THC and potentiated by higher doses of THC. Kinetic analysis suggested that the interaction was of a mixed but predominantly competitive type. THC antagonized the dose dependent PGE1 abdominal constriction response in a fashion which suggested a mixed though mainly competitive antagonism. It would seem that on the two pharmacological parameters studied THC appears to be interacting with PGE1 at the same receptor site. Although the doses of THC used are within the range of those used in man, it is not implied that these results are necessarily implicated in the psychoactivity of the drug. 36 references. (Author abstract modified)

000130 Jakoubek, B.; Petrovicky, P. Institute of Physiology, Czechoslovak Academy of Sciences, Budejovicka 1083, 14220 Prague 4, Czechoslovakia **Incorporation of 4,5-3H-leucine into the neurons of locus ceruleus and other nerve cells in stressed rats: effect of diazepam.** Psychopharmacology (Berlin). 50(2):193-197, 1976.

The incorporation of radiolabeled leucine into neurons of locus ceruleus, neurons of the terminal principal nucleus of the trigeminal nerve and spinal motoneurons was studied in rats subjected to physical stress (S group), rats subjected to physical stress after a single injection of diazepam (DS group) and controls (C group) by quantitative autoradiography. The planimetrically measured neuronal areas of spinal motoneurons and trigeminal neurons were larger in the S group and in the DS group than in the C group. Stress had no effect on neuronal size in locus ceruleus. No significant differences of grain density were found in neurons of the S group and C group; however, diazepam pretreatment markedly increased the grain density in all neurons investigated. It is suggested that the action of benzodiazepine drugs involves the alteration of amino acid metabolism or synthesis of brain proteins as well as changes in catecholamine metabolism. 18 references. (Author abstract modified)

000131 Jansson, S.-E.; Heinonen, E.; Heinanen, V.; Gripenberg, J.; Tolppanen, E.-M.; Salmi, T. Departments of Anatomy and Physiology, University of Helsinki, Siltavuorenpenger, SF-00170 Helsinki 17, Finland **On the effect of the ionophore X-537A on neuromuscular transmission in the rat.** Life Sciences (Oxford). 18(12):1359-1365, 1976.

The effects of X-537A on the release of acetylcholine were investigated using intracellular recording techniques in the rat phrenic nerve diaphragm muscle preparation. The results of this included: 1) depolarized muscle fiber membranes; 2) an occasional transient increase in and ultimate block of spontaneous transmitter relase; 3) no increase in the amplitude of the end plat potential (EPP) but abruptly blocked stimulus evoked transmitter release; and 4) an increase in the occurrence of giant miniature EPP's (MEPP's). The possibility is discussed that the sporadically raised mepp frequency was due to an ionophore induced depolarization of nerve terminals. The increased occurrence of giant MEPP's apparently reflected a X-537A induced spontaneous multiquantal release of acetylcholine. This was not dependent on extracellular calcium but appeared to be of presynaptic origin. 23 references. (Author abstract modified)

000132 Jeppsson, Roland; Ljungberg, Stellan. Dept. of Pharmacology, Faculty of Pharmacy, Univ. of Uppsala, Box 573, S-751 23 Uppsala, Sweden **Anticonvulsant activity in mice of diazepam in an emulsion formulation for intravenous administration.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(4):312-320, 1975.

The anticonvulsant activity of diazepam has been investigated in mice using an electrical low voltage square wave technique. Diazepam was administered intravenously using two injection formulations, Valium and diazepam emulsion. In the latter formulation the lipophilic drug was dissolved in soya bean oil which was then emulsified to an o/w emulsion. A great difference was found in acute intravenous toxicity (LD50) between the two diazepam formulations. The higher toxicity of Valium could probably be due to the solvents used in this formulation. The anticonvulsant activity was about equal for the two preparations. Thus, no difference was found in duration of anticonvulsant activity at the two dose levels and the slopes of the log. dose/response curves did not differ. 17 references. (Author abstract)

000133 Joffe, Justin M.; Mulick, James A.; Peterson, John M.; Paunovic, Jasenka. Department of Psychology, University of Vermont, Burlington, VT 05401 **Sex difference in the effect of dexamethasone on open-field behavior in rats: gonadal hormones.** Physiology & Behavior. 16(5):543-546, 1976.

Because previous experiments indicated that dexamethasone phosphate (DEX) increases open-field defecation in females but not in males, the question of whether this sex difference in response to DEX is due to sex differences in gonadal hormones, female rats were: 1) ovariectomized; 2) ovariectomized and injected with testosterone propionate prior to and during open-field testing; or 3) sham operated. Half the females in each group received DEX in their drinking water during the 4 day period of testing. DEX produced the expected reductions in bodyweight, adrenal weight, and plasma corticosterone levels. Despite the differences between the three groups on a variety of physiological measures, DEX produced comparable increases in open-field defecation in all cases. This indicates that the sex difference in the response of open-field defecation to DEX is not dependent on sex differences in circulating gonadal hormones. 19 references. (Author abstract modified)

000134 Johnson, K. M.; Ho, B. T.; Dewey, W. L. Dept. of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, MCV Station Box 726, Richmond, VA 23298 **Effects of delta9-tetrahydrocannabinol on neurotransmitter accumulation and release mechanisms in rat forebrain synaptosomes.** Life Sciences (Oxford). 19(3):347-356, 1976.

The effects of (-)-delta9-tetrahydrocannabinol (delta9-THC) were studied on the release and accumulation of 3H-5-hydroxytryptamine (3H-5-HT) and 3H-norepinephrine (3H-NE) in a rat forebrain synaptososomal preparation to elevate the possible sites of action of delta9-THC on these two processes. Delta9-THC inhibited the accumulation of 3H-leucine, 3H-leucine, 3H-NE, and 3H-5-HT as well as facilitated the release of

the latter two amines (to a lesser degree), but had no effect on the release of 3H-leucine. Eighteen hour pretreatment with reserpine diminished the ability of delta9-THC to induce release of 3H-5-HT, but had no effect on the in vitro inhibition of synaptosomal uptake of this amine. Concentrations of delta9-THC which blocked the uptake of 3H-5-HT also reduced the conversion of 3H-hyroxy-3-indoleacetic acid (3H-5-HIAA). Delta9-THC, at concentrations which facilitated release of 3H-5-HT from preloaded synaptosomes, increased the amount of 3H-5-HIAA found in the medium. These data suggest that delta9-THC facilitates release from the synaptic vesicle and retards accumulation at the neuronal membrane. 10 references. (Author abstract)

000135 Jones, R. B.; Luscombe, D. K. Welsh School of Pharmacy, UWIST, Cathays Park, Cardiff, Wales **Single dose studies with clomipramine in normal subjects.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):62-67, 1976.

The highly sensitive double radioisotope derivative technique was used to determine the plasma concentrations and urinary excretory pattern of clomipramine and its main breakdown product, N-desmethylchlomipramine, in healthy adults. In volunteer Ss who had received a single 50mg oral dose, clomipramine reached mean peak level in the plasma between 2 and 4 hr after administration, whereas the mean peak level of desmethyclomipramine was reached after 4 to 8 hr. Both compounds were still present in the plasma after 48 hr and could be detected in the urine for up to 14 days. Comment on these observations is included, focusing on methodological questions regarding the assay method and length of time required for side effects of the drug, as well as problems in determining optimal dosage and the therapeutic plasma levels. 13 references. (Author abstract modified)

000136 Jones, R. B.; Luscombe, D. K. Applied Pharmacology Laboratories, Welsh School of Pharmacy, UWIST, Cardiff CF1 3NU, Wales **Plasma levels of clomipramine and its N-desmethyl metabolite following oral administration of clomipramine in man.** British Journal of Pharmacology (Basingstoke). 57(3):430P, 1976.

Plasma concentrations of clomipramine and its N-desmethyl metabolite were determined following oral administration of single or multiple doses. Clomipramine appears rapidly in the plasma after ingestion of a single 50mg oral dose. Peak plasma levels of approximately 37.1ng/ml to 38.1ng/ml occur 2-4 hr after administration. The mean value of individual peak plasma levels is 44.8ng/ml. Desmethylclomipramine is not detected in plasma until 1 hr after administration. Maximum plasma concentrations of 0.5ng/ml to 12.0ng/ml occur between 4 hours and 24 hours after administration. Parent drug and metabolite are detectable in plasma 48 hours after ingestion, indicating relatively long plasma half-lives for both substances. Clomipramine was also administered at a dose of 25mg 3 times daily for 4 weeks. Steady state plasma levels are reached within 7 days. Mean individual plasma concentrations ranged in this study from 21.4ng/ml to 68.7ng/ml at day 28. Marked individual variation in the ratio between drug and metabolite in plasma indicate that individual patients vary in ability to metabolize clomipramine. In the majority of patients, plasma levels of metabolite are greater than those of parent drug. It is suggested that desmethylclomipramine may be a major contributory factor in the overall antidepressant effect of clomipramine. References.

000137 Jun, H. W. Department of Pharmacy, School of Pharmacy, University of Georgia, Athens, GA 30602 **Pharmacokinetic studies of pentylenetetrazol in dogs.** Journal of Pharmaceutical Sciences. 65(7):1038-1041, 1976.

Pharmacokinetic profiles of pentylenetetrazol in the dog were studied following rapid intravenous and oral administrations of a convulsant dose (15-20mg/kg). Plasma level time curves after a rapid intravenous injection showed biexponential decline, indicating that the disposition of this drug in the dog follows a two compartment body model. Pharmacokinetic parameters were calculated from the intravenous data. After oral administration of the solution dose, the peak plasma level appeared at about 30 min postdose, indicating that the absorption occurs rapidly. Areas under the oral plasma level time curves showed that the drug was absorbed completely and that the first pass metabolism effect was minimal. Ligation studies of the kidney and the liver suggested that the main elimination pathway of this drug was biotransformation in the liver. The average plasma half-life was 1.4hr. At steady state, the volume of distribution was approximately equivalent to the volume of the total body water. 10 references. (Author abstract)

000138 Juorio, A. V. Psychiatric Research Unit, University Hospital, Saskatoon, Saskatchewan, S7N OW8, Canada **Presence and metabolism of beta-phenylethylamine, para-tyramine, meta-tyramine and tryptamine in the brain of the domestic fowl.** Brain Research (Amsterdam). 3(2):442-445, 1976.

A study was carried out to: 1) identify and measure beta-phenybthylamine, para-tyramine, meta-tyramine and trypotamine in the brain of domestic fowl; 2) determine the changes in these amines produced by the administration of a monoamine oxidase (MAO) inhibior; and 3) measure the concentrations of dopamine, noradrenaline, adrenaline and 5-hydroxytryptamine (5-HT) for comparative purposes. The concentrations of beta-phenylethylamine, meta-tyramine and para-tyramine range from 0.3ng/g to 0.71ng/g; the concentration of tryptamine is less than 0.3ng/g. The concentrations of dopamine, noradrenaline and 5-HT are approximately 100 fold higher, the concentration of adrenaline is approximately intermediate between the two groups of amines. Administration of pargyline, a MAO inhibitor, increases the concentration of beta-phenylithylamine 34 fold, para-tyramine 23 fold, m-tyramine 4.4fold and tryptamine more than 48 fold. Pargyline increases the concentration of dopamine, noradrenaline and adrenaline by 10% to 20% but produces a significant increase in 5-HT concentration (approximately 90%). 19 references.

000139 Karasawa, Tadahiko; Furukawa, Kiyoshi; Yoshida, Kouichi; Shimizu, Masanao. Department of Pharmacology, Research Laboratories, Dainippon Pharmaceutical Co. Ltd., Suita, Osaka, 564, Japan **Effect of theophylline on monoamine metabolism in the rat brain.** European Journal of Pharmacology (Amsterdam). 37(1):97-104, 1976.

The effect of theophylline on brain monoamine metabolism was studied in rats. Single doses of theophylline cause a striking and dose related increase in the levels of 3-methoxy-4-hydroxyphenylethylene glycol sulfate (MOPEG-S04) and 5-hydroxyindoleacetic acid (5-HIAA) in the brain. The level of brain homovanillic acid is only slightly affected. No appreciable change occurs in the levels of brain norepinephrine, serotonin and dopamine. The increased level of brain MOPEG-SO4 or 5-HIAA after theophylline does not appear to result from its interference with the transport system for the acids in the brain since the rate of decline of the acid levels following pargyline is not affected. Under the conditions of brain monoamine oxidase inhibition, theophylline enhances the increase in brain normatanephrine level without causing any

change in 3-methoxytyramine level. The enhancement of brain normetanephrine level by theophylline is more pronounced when rats are pretreated with imipramine in addition to pargyline. These results suggest that, in the brain, theophylline may cause a release of serotonin leading to its increased turnover. The results also confirm the previous conclusion that the methylxanthine causes a release of norepinephrine and a concomitant increase in its turnover in the brain. 14 references. (Author abstract modified)

000140 Kerr, D. I. B.; Dennis, Barbara J.; Breuker, Elisabeth L. M.; Prager, R. H.; Ward, A. D.; Duong, Thach. Department of Human Physiology and Pharmacology, University of Adelaide, Adelaide 5001, Australia **Antagonism of GABA-mediated inhibition in the central nervous system by caprolactam derivatives.** Brain Research (Amsterdam). 110(2):413-416, 1976.

The effects of picrotoxin, caprolactam, and two caprolactam derivatives (4,6,6-trimethyl caprolactam and 1,5,6,7-tetrahydro-4,6,6-trimethyl-2H-azepin-2-one) on the positive field potentials evoked in the substantia nigra by striopallidal stimulation were studied in rabbits. Conventional monopolar recording from the substantia nigra was performed. Responses were evoked with bipolar stimulation of the striopallidum at 3 sec. Convulsant doses of all drugs tested block the positive field potentials in the substantia nigra. It is suggested that the caprolactams produce their effects by antagonism of GABA mediated central nervous system (CNS) inhibition of convulsant activity rather than by a direct excitatory effect on CNS neurones. The nature of the GABA receptor and the active configuration of the GABA molecule are discussed. 12 references.

000141 Kim, Kyung Hee. Department of Neuropsychiatry, Yonser University Medical College, Korea **Effects of haloperidol and lithium on blood alcohol level in rabbits.** Neuropsychiatry (Seoul). 14(3):260-268, 1975.

The effects of haloperidol and lithium, alone or in combination, on the blood alcohol level in rabbits were studied. Mature rabbits of both sexes were used for both experimental and control groups. The results obtained are as follows: 1) the orally administered haloperidol (2mg/kg/day for 5 days and 10 days) elevated significantly the blood alcohol level in rabbits 15 mins after the administration of alcohol; 2) the intravenous injection of lithium chloride (3mEq/kg/day for 4 days) elevated significantly the blood level in rabbits both 15 and 45 mins after the administration of alcohol; 3) the haloperidol combined with lithium chloride (2mg/kg/day and 4mg/kg/day respectively for 5 days) lowered significantly the blood alcohol level 45 mins after the administration of alcohol; and 4) the haloperidol combined with lithium chloride (2mg/kg/day and 4mg/kg/day respectively for 10 days) lowered significantly the blood alcohol level both 15 and 45 mins after the administration of alcohol. 34 references. (Author abstract modified)

000142 Klemm, W. R.; Dreyfus, L. R.; Forney, E.; Mayfield, M. A. Department of Biology, Texas A and M University, College Station TX 77843 **Differential effects of low doses of ethanol on the impulse activity in various regions of the limbic system.** Psychopharmacology (Berlin). 50(2):131-138, 1976.

The effects of various doses of alcohol on electroencephalogram (EEG) and multiple unit activity (MUA) recorded from nine brain areas including the hippocampal cortex, some of its associated input structures, and different zones within the hippocampus proper were studied in rabbits. Subjective evaluation of EEG tracings from all brain areas did not disclose any regional differences. The incidence of hippocampal theta rhythm was depressed transiently with lower doses of ethanol, but was increased in some animals following the largest dose. A predominant depression of MUA occurred in the septum, fimbria/fornix, entorhinal cortex and CA-1 zone of the hippocampus. Large transient increases in MUA were noted in the CA-1, hippocampal commissure and entorhinal cortex. Overall, regional differences in unit activity consisted of a relatively greater effect in the septum, CA-1, and the entorhinal cortex while conspicuously smaller effects were evident in the CA-3 zone and dentate zone of the hippocampus. It is suggested that additional support has been given to the hypothesis that ethanol has preferential actions on certain kinds of neurons. 18 references. (Author abstract modified)

000143 Knapp, Suzanne; Mandell, Arnold J. Department of Psychiatry, M-003, University of California at San Diego, School of Medicine, LaJolla, CA 92093 **Coincidence of blockade of synaptosomal 5-hydroxytrysptamine uptake and decrease in tryptophan hydroxylase activity: effects of fenfluramine.** Journal of Pharmacology and Experimental Therapeutics. 198(1):123-132, 1976.

The effects of fenfluramine in the coincidence of blockade of synaptosomal 5-hydroxytryptamine uptake and decrease in tryptophan hydroxylase activity (5-HT) were studied in vitro. A single injection of fenfluramine hydrochloride resulted in a short-term increase in striate synaptosomal conversion of tryptophan to serotonin (5-HT) in rat brain. In contrast, D-and L-amphetamine sulfate resulted in a short-term decrease of this index of 5-HT biosynthesis. None of the amphetamines studied altered the kinetics of synaptosomal uptake of L-(3-14C)-tryptophan measured in the same striate preparation. Within 4 hours after fenfluramine administration, 3H-5-HT uptake into synapsosomes was markedly decreased; it returned to control levels in 10 to 14 days. Intrasynaptosomal tryptophan hydroxylase activity dropped markedly within 4 hours of drug administration and remained depressed for 10 to 14 days, its return to control levels coinciding with that of 3H-5-HT uptake. Only 5-HT cell body enzyme prepared from the lateral midbrain (B9) demonstrated a reduction in activity comparable to that seen in the synaptosomes; very small decreases occurred in cell body enzyme prepared from whole midbrain (B7, B8, B9) or medial midbrain (B7,B8). Lateral midbrain tryptophan hydroxylase activity returned to control levels by 8 days. In vitro, fenfluramine affected none of these indices of central 5-HT biosynthesis persisted longer that those of D-amphetamine, which lasted less than 24 hours. However, the fenfluramine effects were much shorter than those reported for P-chloroamphetamine, which persist for up to 3 months. These three amphetamines apparently affect the lateral midbrain raphe nuclei selectively. 34 references. (Author abstract modified)

000144 Koss, Michael C. Dept. of Pharmacology, University of Oklahoma College of Medicine, Oklahoma City, OK 73190 **Studies on the site of action of clonidine utilizing a sympathetic-cholinergic system.** European Journal of Pharmacology (Amsterdam). 37(2):381-384, 1976.

The sympathetic cholinergic system was used in the analysis of the site of the sympatho inhibitory action of clonidine in 30 adult cats. Clonidine (30mg/kg intravenously) reduced centrally evoked electrodermal responses (EDR) following stimulation of reactive loci in the hypothalamus medulla. The responses were most depressed following low frequency stimulation. Similar results were observed on the EDR evoked by stimulation of the cervical cord in the spinal cat. Little effect was seen following peripheral nerve stimulation. These results

demonstrate that clonidine depresses the reactivity of this sympathetic cholinergic system at all central levels including the cervical cord. 10 references. (Author abstract modified)

000145 Kraemer, Gary W.; Mueller, Robert; Breese, George R.; Prange, Arthur J.; Lewis, Jonathan K.; Morrison, Helen; McKinney, William T., Jr. Primate Laboratory and Research Institute, University of Wisconsin, Medical School, Madison, WI 53706 **Thyrotropin releasing hormone: antagonism of pentobarbital narcosis in the monkey.** Pharmacology Biochemistry and Behavior. 4(6):709-712, 1976.

The effect of thyrotropin releasing hormone (TRH) on pentobarbital narcosis in 12 rhesus monkeys was examined. Vital signs monitored included respiration rate, heartrate, temperature, sleeping time, and time of reappearance of certain reflexes. Blood samples were obtained for pentobarbital assay. TRH administration resulted in dramatically increased respiration and heartrates and arrested the progress of barbiturate induced hypothermia. The extended dose schedule prolonged increased respiration rate and a differential effect of TRH on pentobarbital induced hypothermia across sexes was observed. All animals regained reflexes sooner and sleeping time was reduced by 22%. These results extend earlier work in rodents to primates and suggest a possible use of TRH in cases of acute barbiturate intoxication. 10 references. (Author abstract modified)

000146 Kruse, Hansjorg. Hansjorg Kruse, Abt. fur Pharmakologie, Hoechst AG, D-6230 Frankfurt a. M.-80, Postfach 800320, Germany **Thyrotropin releasing hormone (TRH): restoration of oxotremorine tremor in mice.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(1):39-45, 1976.

The mode of action of thyrotropin releasing hormone (TRH) in comparison to quipazine was investigated. Both TRH and quipazine were found to restore and to intensify the oxotremorine induced tremor in mice when injected i.p. 60 min after oxotremorine O.5mg/kg s.c. Also other dopaminergic drugs (e.g. amphetamine, methylphenidate, nomifensine and apomorphine) had a significant but lesser effect than TRH or quipazine. Based upon these and other results it is concluded that quipazine exerts its effect by direct stimulation of serotoninergic and dopaminergic receptors, whereas TRH receptors may represent separate entities and TRH may function as a neurotransmitter or neuromodulator. 13 references. (Author abstract modified)

000147 Kuroda, Shigetoshi. Department of Neuropsychiatry, Okayama University Medical School, Okayama, Japan **Ultrastructural studies of chloramphenicol-induced neuropathy in experimental animals.** Brain and Nerve (Tokyo). 27(3):309-315, 1975.

Chloramphenicol (CP) was given to dogs and rabbits to check the neuropathological results. The drug was administered over periods of 60 to 108 days both orally and by intramuscular injection. Results were observed under light and electron microscopes. In sural nerves, changes in the myelin sheaths and Schwann cells were prominent. Myelin sheaths swelled or enlarged, while Schwann cells both enlarged and increased in number. Several intracellular changes were also observed. In the lumbar root ganglia, nerve cells showed various changes: the cisternae of endoplasmic reticuli were irregularly swollen, mitochondria showed derangement of the direction of the cristae, and neurofilaments variously increased or decreased in number. The nuclei showed indentations of the nuclear membrance accompanied by nuclear pores densely patched on the membrane surface. No pathological changes were noted in the lining cells. 28 references. (Author abstract modified)

000148 Kuschinsky, K. Max-Planck-Institut fur experimentelle Medizin, Abt. Biochemische Pharmakologie, Hermann-Rein-Str. 3, D-3400 Gottingen, West Germany **Actions of narcotics on brain dopamine metabolism and their relevance for "psychomotor" effects.** Arzneimittel-Forschung (Aulendorf). 26(4):563-567, 1976.

The effects of narcotic analgesics, particularly of morphine, on dopamine metabolism in the corpus striatum, and the correlation of these effects to motility and psychomotor phenomena are reviewed. In rats, acute doses of morphine decrease dopaminergic neurotransmission in the brain without blocking the postsynaptic dopamine receptors. Chronic treatment of rats with morphine reverses these acute effects of morphine and induces symptoms of increased dopaminergic neurotransmission in the brain. In mice and cats, on the other hand, acute doses of morphine apparently increase dopaminergic neurotransmission. The effects of morphine on striatal dopamine metabolism seem to be a model well suited to study opioid specific effects on a cellular level. Furthermore, they might be responsible for some narcotic specific effects on behavior observed in animals and man. 81 references. (Author abstract modified)

000149 Ladinsky, H.; Consolo, S.; Bianchi, S.; Peri, G.; Garattini, S. Istituto di Ricerche Farmacologiche "Mario Negri," Via Eritrea, 62, I-20157 Milano, Italy **Lack of influence of the phase of estrus cycle or treatment with steroid contraceptive drugs on cholinergic parameters in mouse and rat brain.** Pharmacology (Basel). 14(3):232-239, 1976.

An investigation was carried out to determine whether brain area acetylcholine levels, choline levels and choline acetyltransferase activity fluctuate in mice and rats with the phase of the estrus cycle and whether subchronic treatment or chronic treatment with steroid contraceptive drugs affect these cholinergic parameters. Acetylcholine levels and choline levels in the cerebral hemispheres, diencephalon and mesencephalon of the rat and mouse do not fluctuate with the phase of the estrus cycle. Choline acetyltransferase activity is not altered in these brain areas in the mouse, but in the rat there is a small but significant decrease in the cerebral hemispheres during proestrus and in the mesencephalon during estrus, both with respect to diestrus. Chronic 30 day treatment with steroid contraceptive drug combinations (lynestrenol 5mg/kg and mestranol 0.3mg/kg, lynestrenol 2.5mg/kg and mestranol 0.15mg/kg, norethindrone 4mg/kg and mestranol 0.02mg/kg and norethynodrel 4mg/kg and mestranol 0.06mg/kg) does not alter cholinergic parameters in the brain areas of mouse or rat except for minor changes in rare instances. 15 references. (Author abstract modified)

000150 Lau, C.; Slotkin, T. A. Department of Physiology and Pharmacology, Duke University Medical Center, Durham, NC 27710 **Indirect and direct inhibition of dopamine beta-hydroxylase by amphetamine in storage vesicles and synaptosomes.** British Journal of Pharmacology (London). 57(2):223-228, 1976.

The mechanism by which amphetamine produces a functional inhibition of dopamine beta-hydroxylase (DBH) was studied by examination of the effect of amphetamine on amine uptake and on beta-hydroxylation in isolated adrenal storage vesicles and in whole brain synaptosomes of the rat. Amphetamine produces a competitive inhibition of catecholamine incorporation into adrenal vesicles with a Ki of 279 micromols. This action of the drug accounts for slightly

less than half of the total inhibition of beta-hydroxylation in the vesicles, indicating that the interference by amphetamine of access of substrate to the enzyme compartment plays an important role in functional inhibition of DBH. The remainder of the effect in vesicles probably represents direct inhibition of the enzyme. In whole brain synaptosomes, similar actions on uptake of substrate and on functional enzyme activity are noted, indicating that amphetamine induced inhibition of the neuronal amine pump can also affect DBH activity if the substrate is supplied exogenously. Chronic administration of amphetamine to rats produces an increase in total activity of adrenal DBH. It is concluded that the net effect of amphetamine on DBH activity respresents the summation of direct inhibition of the enzyme, indirect inhibition via reduced access of substrate and enhancement of activity via transsynaptic induction. 29 references. (Author abstract modified)

000151 Lauressergues, Henri; Stenger, Antoine; Culetto, Marie; Mouzin, Gilbert; Cousse, Henri. Centre de Recherche Pierre Fabre S. A., 17, Avenue Jean Moulin, 81106 Castres, France **/Influence on psycholeptic effects of different types of substitutions in a series of cresotinic amides./** Influence sur les effets psycholeptiques de differents types de substitutions dans une serie d'amides cresotiniques. European Journal of Medicinal Chemistry (Paris). 10(6):629-632, 1975.

A series of differently substituted cresotinic amides was studied. Influence on psycholeptic effects of substituents according to their nature and position was determined. Derivatives with bromine in para-position of the phenol group have proved to be less toxic than chloroderivatives. Bromo-5N-isopropyl ortho cresotinamides was the most active derivative according to myroelaxant properties, potentiation of neurobarbital or chloral induced narcosis and anticonvulsive effect. Positive influence of monosubstitution by a group hindered at the nitrogen level can be explained in studying metabolic pathways of such derivatives. 24 references. (Journal abstract)

000152 Leander, J. David; McMillan, D. E.; Ellis, F. W. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Ethanol and isopropanol effects on schedule-controlled responding.** Psychophamacology (Berlin). 47(2):157-164, 1976.

The effects of ethanol and isopropanol were studied on responding by pigeons under multiple fixed-ratio (FR), fixed-interval (FI) schedules of food presentation and under a fixed-interval (FI) schedule of food presentation where responding was decreased by punishment. The ethanol was rapidly absorbed into blood and decreased responding within 15 min after intubation to the opening of the proventriculus. Dose effect determinations of the effects of ethanol showed that ethanol decreased responding in both the FR and FI components of the multiple schedules at similar doses, but there were increases in responding under an FR 100 schedule at lower doses. Isopropanol tended to decrease FR responding at doses that either increased FI responding or did not affect FI responding. Both ethanol and isopropanol (1g/kg) produced effects on the local rates of responding within the FI which were rate dependent in that they increased low rates while not affecting or actually decreasing the high rates of responding. Both ethanol and isopropanol increased punished responding if it was not severely suppressed by the punishment procedures. 40 references. (Author abstract)

000153 Lee, Cheng-Yi; Akera, Tai; Brody, Theodore M. Department of Pharmacology, University of California, San Francisco, CA 94143 **Comparative effects of chlorpromazine and its free radical on membrane functions.** Biochemical Pharmacology (Oxford.). 25(15):1751-1756. 1976.

Chlorpromazine, chlorpromazine free radical and a sulfhydryl inhibitor, p-hydroxymercurie benzoate, were compared for their effects on several biochemical phenomena associated with membrane function. Chlorpromazine free radical was slightly more potent than chlorpromazine in inhibiting calcium accumulation by rat brain microsomes, but less potent in protecting synaptosomes from osmotic shock, and in inhibiting synaptosomal uptake of dopamine and norepinephrine. p-Hyroxymercuribenzoate failed to protect synaptosomes from osmotic shock. It was less effective than chlorpromazine and chlorpromazine free radical in inhibiting synaptosomal uptake of dopamine and norepinephrine are caused by chlorpromazine itself but not by chlorpromazine free radical. Although chlorpromazine free radical was a more potent inhibitor of synaptosomal calcium uptake than chlorpromazine, the differences in potency were markedly smaller than those on microsomal Naionkion-ATPase previously reported. 35 references. (Author abstract)

000154 Leonard, B. E.; Kafoe, W. F. Pharmacology Department, University College, Galway, Ireland **A comparison of the acute and chronic effects of four antidepressant drugs on the turnover of serotonin, dopamine and noradrenaline in the rat brain.** Biochemical Pharmacology (Oxford). 25(17):1939-1942, 1976.

The acute effects of imipramine, Org GB 94, and iprindol, and the chronic effects of imipramine, desipramine, iprindol, and Org GB 94 were studied on the turnover of dopamine, noradrenaline, and serotonin in the whole rat brain. The effects of these drugs on amine turnover was assessed from the incorporation of tritiated tyrosine and tritiated tryptophan into the amines. Following acute administration, imipramine significantly reduced the turnover of serotonin whereas Org GB 94 increased that of noradrenaline. After chronic administration, imipramine and desipramine reduced the turnover of serotonin ad dopamine, iprindol had no significant effect on brain amine turnover, and Org GB 94 increased the turnover of noradrenaline. The effect of Org GB 94 on noradrenaline turnover was more marked after intraperitoneal administration than after oral administration. 22 references. (Author abstract)

000155 Lew, J. Y.; Miyamoto, T.; Goldstein, M. N. Y. U. Medical Center, Dept. of Psychiatry, Neurochemistry Laboratories, 550 Fifth Avenue, New York, NY 10016 **Inhibition of PNMT activity in the adrenal glands and brain stem of rats.** Biochemical Pharmacology (Oxford). 25(12):1433-1434, 1976.

The effects of several phenylethanoalamine N-methyltransferase (PNMT) are described on the in vivo and in vitro activity of PNMT in the brain. The immunofluorescence technique was used to map out the PNMT neuronal system in the central nervous system of rats. The effects of several PNMT inhibitors on the activity of the enzyme isolated from rat adrenals and the brain are summarized in tabular form. 15 references.

000156 Lorez, Hanspeter; Saner, Alphonse; Richards, John G.; Da Prada, Mose. Department of Experimental Medicine, F. Hoffmann-La Roche, Basel, Switzerland **Accumulation of 5-HT in non-terminal axons after p-chloro-N-methylamphetamine without degeneration of identified 5-HT nerve terminals.** European Journal of Pharmacology (Amsterdam). 38(1):79-88, 1976.

The effect of a single injection of d,l-p-chloro-N-methylamphetamine (PCMA) on 5-hydroxytryptamine (5-HT) containing neurons in rat brain was investigated with fluorescence histochemical, electron microscopic and biochemical methods. PCMA induces a transient accumulation of 5-HT in nonterminal axons probably by disturbing axoplasmic flow in these neurons. This effect may be useful in the mapping of 5-HT nerve fiber pathways in the central nervous system. Although such an accumulation could imply that damage to 5-HT nerve terminals has also occurred, there is no ultrastructural evidence to support this interpretation. Neither were there definite morphological changes in 5-HT cell bodies, so that a severe neurotoxic action on 5-HT neurons seems not to be causal for the long-term reduction in 5-HT content of the brain. 41 references. (Author abstract modified)

000157 Mackerer, Carl R.; Clay, George A.; Dajani, Esam Z. Pharmacodynamics Section, Department of Biological Research, Searle Laboratories, Box 5110, Chicago, IL 60680 **Loperamide binding to opiate receptor sites of brain and myenteric plexus.** Journal of Pharmacology and Experimental Therapeutics. 199(1):131-140, 1976.

Loperamide was tested to determine whether its biological activity involves binding to opiate receptor sites. Loperamide and morphine competitively inhibited 3H-naloxone binding to homogenates of guinea-pig brain and myenteric plexus. In the absence of Na+, binding of loperamide and morphine to brain homogenate was enhanced while the binding of naloxone was reduced. In the mouse hot plate test, subcutaneous administration of morphine and loperamide delayed the response to heat stimuli and this effect was completely blocked by prior administration of naloxone. In the anesthetized dog, intravenous administration of morphine and loperamide enhanced the contractile activity of circular muscle in proximal and distal duodenum, distal ileum, and proximal colon, but duodenal longitudinal muscle was relaxed; these effects were completely reversed by subsequent administration of naloxone. It is concluded that loperamide binds to opiate receptor sites and possesses opiate agonist activity both in vivo and in vitro. 33 references. (Author abstract modified)

000158 MacKinnon, A. M.; Simon, F. R. Division of Gastroenterology, University of Colorado Medical Center, Denver, CO 80220 **Impaired hepatic heme synthesis in the phenobarbital-stimulated selenium-deficient rat (39442).** Proceedings of the Society for Experimental Biology and Medicine. 152(4):568-572, 1976.

The effects of phenobarbital on hepatic heme synthesis and on apoprotein synthesis in selenium deficient rats were investigated. Phenobarbital induced increases in heme synthesis were lower in selenium deficient animals than in selenium replete animals. However, the phenobarbital induced increase in cytochrome P-450 apoprotein was not impaired in the selenium deficient animals. It is concluded that in selenium deficient animals, the synthesis of the heme moiety and the apoprotein moiety of cytochrome P-450 do not respond identically to phenobarbital induction. 20 references.

000159 Majkowski, Jerzy; Sobieszek, Aleksander; Bilinska-Nigot, Barbara; Karlinski, Andrzej. Department of Neurology, Research and Didactic Center of Medical Academy, 04-073 Warsaw, Grenadierow 51, Poland **EEG and clinical studies of the development of alumina cream epileptic focus in split-brain cats.** Epilepsia (Amsterdam). 17(3):257-269, 1976.

The development of electrophysiological and clinical manifestations of epileptic focus in split brain cats after alumina cream injection in the sensorimotor cortex is reported, and observations on the effects of diphenylhydantoin on epileptic activity and clinical seizures are carried out. Alumina cream epileptic focus was established in the right sensorimotor cortex in 20 split brain cats (partial or complete). Four types of EEG changes after alumina cream injection were differentiated. These types could be related to the direct effects of brain-damage and to development of epilepsy. Diphenylhydantoin failed to prevent or control the epileptic processes. It is concluded that the antiepileptic properties of diphenylhydantoin are counteracted by its toxic effects in cats with well developed biolectrical epileptic focus. 21 references.

000160 Malmnas, Carl Olof. Department of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **The significance of dopamine, versus other catecholamines, for L-dopa induced facilitation of sexual behavior in the castrated male rat.** Pharmacology Biochemistry and Metabolism. 4(5):521-526, 1976.

The effects of a wide dose range of L-DOPA on male rat sexual behavior were investigated. The animals were castrated as adults and supplied with small amounts of testosterone propionate. Doses of L-DOPA up to 2.5mg/kg facilitated, while higher doses inhibited, sexual behavior in animals pretreated with the monoamine oxidase inhibitor pargyline, 20mg/kg, plus the extracerebral decarboxylase inhibitor MK486, 50mg/kg. The effects of L-DOPA on sexual behavior were not restricted to the copulatory act, but included elements preceding the copulatory act as well. Most of the facilitatory effects of L-DOPA 2.5mg/kg were prevented by the dopamine receptor blocker pimozide, facilitation of sexual behavior in the castrated male rat. However, some elements of the copulatory act appear to be modified by noradrenaline and/or adrenaline as well. 16 references. (Author abstract modified)

000161 Manara, L.; Cerletti, C.; Mennini, T. Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, I-20157 Milan, Italy **Prevention by calcium administration of reserpine action on rat brain noradrenaline stores: a reappraisal.** Research Communications in Chemical Pathology and Pharmacology. 14(3):471-487, 1976.

The conditions under which pretreatment with a calcium salt may prevent the action of reserpine on brain noradrenaline stores in the rat were investigated. Results show that only after subcutaneous administration of reserpine in the same site as a previous CaCl2 injection, was the action of reserpine prevented and reduced levels of this drug were found in the brain. Depletion of encephalic noradrenaline following reserpine, as well as the reserpine brain concentration, were not affected by subcutaneously administered calcium chloride, when reserpine was administerd either intraveneously or subcutaneously in a site different from that selected for pretreatment with the calcium salt. In essence calcium chloride, a well known irritant, acts at the site of subcutaneous administration, thus limiting by a nonspecific mechanism the absorption of reserpine. Under similar conditions, the absorption of harmaline was likewise altered. It is suggested that the significance of some studies on calcium/reserpine interaction should be reappraised. 17 references. (Author abstract modified)

000162 Mandell, Arnold J. Department of Psychiatry, School of Medicine, University of California, San Diego, La Jolla, CA 92037 **Neurobiological mechanisms of adaptation in relation to models of psychobiological development.** In: Schopler, E.,

Psychopathology and child development. New York, Plenum, 1976. 395 p. (p. 21-31).

To demonstrate neurochemical mechanisms of adaptation in relation to psychobiological development, preclinical studies of macromoleculr adaptive changes in brain adrenergic and serotonergic neurons are reviewed. Focusing on responses to drug administration primarily in rodents, a series of processes in adult and neonate Ss are described, ranging from alterations in receptor sensitivity, biosynthetic enzyme activity in nerve endings and the uptake, degradation and flow rate by which enzymes synthesized in the nucleus are transported to the nerve ending where they function. A model of a homeostatic mechanisms that produces a defensive, compensatory response to state deviations in the adult organism is developed. The mature organism can maintain its baseline state in response to deviations of external or internal environment. When the irregularity or change is removed, the neuronal system returns to baseline. The developing organism, however, is susceptible to more lasting changes in response to experienced perturbations. If the baseline homeostatic mechanism is established during a critical period when sensitive to direct effects (drug, hormones, etc.)and experimental conditions (stimulus deprivation), metabolic adaptive regulation may be permanent. Findings have broad implications for clinical neurobiology. 15 references.

000163 Mantle, Timothy J.; Tipton, Keith F.; Garrett, Nigel J. Department of Biochemistry, Tennis Court Road, Cambridge CB2 1QW, England **Inhibition of monoamine oxidase by amphetamine and related compounds.** Biochemical Pharmacology (Oxford). 25(18):2073-2077, 1976.

A detailed kinetic study was carried out to determine the effects of several alpha-methyl amines on monoamine oxidase activity over a range of substrate concentrations and inhibitor concentrations. Alpha-methylbenzylamine, alpha-methyltrypamine and the two stereoisomers of amphetamine were shown to be competitive inhibitors of the oxidation of benzylamine, tyramine and serotonin by rat liver monoamine oxidase. All these compounds were more potent inhibitors of serotonin oxidation than of benzylamine oxidation, with alpha-methyl-tryptamine showing the greatest selectivity and alpha-methylbenzylamine the least. The kinetics of the inhibition of tyramine oxidation were consistent with the presence of two enzyme species with different inhibitor sensitivities which were both active towards this substrate. The selectivity of these inhibitors was demonstrated with membrane bound and solubilized preparations of the enzyme, but it could be abolished by treatment of the latter preparation with the chaotropic agent sodium perchlorate. The significance of monoamine oxidase inhibition in connection with the pharmacological action of amphetamine is discussed. 38 references. (Author abstract modified)

000164 Martin, W. R.; Eades, C. G.; Thompson, J. A.; Huppler, R. E.; Gilbert, P. E. NIDA Addiction Research Center, P.O. Box 12390, Lexington, KY 40511 **The effects of morphine- and nalorphine-like drugs in the nondependent and morphine-dependent chronic spinal dog.** Journal of Pharmacology and Experimental Therapeutics. 197(3):517-532, 1976.

The hypotheses that morphine and related drugs are agonists, and that they exert their agonistic actions by interacting with several categories of receptors to produce distinguishable pharmacologic syndromes were examined. Three different syndromes produced by congeners of morphine have been identified in the nondependent chronic spinal dog. These syndromes have been attributed to interactions of agonists with three distinguishable receptors (mu, kappa and sigma). Morphine is the prototype agonist for the mu receptor, ketocyclazocine for the kappa receptor and SKF-10,047 for the sigma receptor. The morphine syndrome (mu) in the dog is characterized by miosis, bradycardia, hypothermia, a general depression of the nociceptive responses and indifference to environmental stimuli. Ketocyclazocine (kappa) constricts pupils, depresses the flexor reflex and produces sedation but does not markedly alter pulse rate or the skin twitch reflex. SKF-10,047 (sigma), in contrast to morphine and ketocyclazocine, causes mydriasis, tachypnea, tachycardia and mania. The effects of these three drugs can be antagonized by the pure antagonist naltrexone, indicating that they are agonists. Further, chronic administration of morphine, ketocyclazocine and SKF-10,047 induces tolerance to their agonistic effects. Morphine suppresses abstinence in morphine dependent dogs while ketocyclazocine does not. Ketocyclazocine at best precipitated only a liminal abstinence syndrome in the morphine dependent dog, indicating that it had little affinity for the morphine receptor. Ketocyclazocine appears to be a selective agonist at the kappa receptor. Further, it has been shown that buprenorphine is a partial agonist of the mu type which both suppressed and precipitated abstinence in the morphine dependent dog while morphine and propoxyphene are stronger agonists. Apomorphine and SKF-10,047 produce similar pharmacologic effects suggesting that sigma activity may involve a dopaminergic mechanism. 28 references. (Author abstract modified)

000165 Masek, K.; Kadlecova, O.; Poschlova, N. Institute of Pharmacology, Czechoslovak Academy of Sciences, Prague, Czechoslovakia **Effect of intracisternal administration of prostaglandin E1 on waking and sleep in the rat.** Neuropharmacology (Oxford). 15(8):491-494, 1976.

The effect of intracisternal administration of prostaglandin E1 (PGE1) on different forms of sleep was investigated in order to validate the original observation of Haubrich et al (1973) and to determine whether the central noradrenergic neurones are involved in the effect of prostaglandin. Intracisternal injection of PGE1 to rats was followed by a marked decrease of the paradoxical phase of sleep in the 2nd and 3rd hour after prostaglandin injection. The administration of 6-hydroxydopamine, which lowered the total level of noradrenaline to 40% of control value and dopamine to 50% of control value, decreased the total time the animals spent in paradoxical sleep by 50%. The injection of PGE1 to 6-hydroxydopamine treated rats further decreased the time that animals spent in paradoxical PGE1 sleep. However, the total time of paradoxical sleep in intact and 6-hydroxydopamine treated animals injected with PGE was about equal, i.e. 10% to 15% of control values. It is suggested that at least part of the effect of PGE1 on sleep patterns might be related to an effect on noradrenergic neurones; however, the possible involvement of other systems cannot be excluded. 17 references. (Author abstract modified)

000166 Matheson, R. T.; Herbst, J. J.; Jubiz, W.; Freston, J. W.; Tolman, K. G. University of Utah College of Medicine, Salt Lake City, UT 84132 **Absorption and biotransformation of cholecalciferol in drug-induced osteomalacia.** Journal of Clinical Pharmacology. 16(8-9):426-432, 1976.

Four patients with osteomalacia and three controls were studied to determine if abnormal gastrointestinal absorption of vitamin D3 and/or biotransformation of D3 to 25-hydroxycholecalciferol (25-OHD3) are present in patients with drug induced osteomalacia. The mean coefficient of absorption was virtually identical in the drug treated group and the control

group. The biotransformation of vitamin D3 to 25-OHD3 was significantly accelerated in the drug treated group compared to the control group. These data suggest that vitamin D absorption is not significantly altered but that biotransformation of vitamin D3 to 25-OHD3 is accelerated in drug induced osteomalacia. 24 references.

000167 Matsuzaki, Masaji; Spingler, Philip J.; Misra, Anand L.; Mule, Salvatore J. New York State Office of Drug Abuse Services, Testing and Research Laboratory, 80 Hanson Place, Brooklyn, NY 11217 **Cocaine: tolerance to its convulsant and cardiorespiratory stimulating effects in the monkey.** Life Sciences (Oxford). 19(2):193-203, 1976.

Evidence for the development of tolerance to the convulsant and cardiorespiratory stimulating effect of cocaine in the monkey is presented. Repeated daily intravenous injections of cocaine in the monkey at a minimal convulsant dosage (MCD) produced tolerance resulting in a marked increase in the MCD of cocaine. The repeated daily intraveouous injections of cocaine at subconvulsant doses produced a marked decrease in the cardiorespiratory stimulating effect and apparent plasma half-life of cocaine in the monkey. The mechanisms effecting these changes were not determined. 22 references. (Journal abstract modified)

000168 Meek, James L.; Lofstrandh, Sonja. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Tryptophan hydroxylase in discrete brain nuclei: comparison of activity in vitro and in vivo.** European Journal of Pharamcology (Amsterdam). 37(2):377-380, 1976.

The accumulation of 5-hydroxytryptophan (5-HTP) in discrete nuclei after treatment of the rats with the decarboxylase inhibitor Ro 4/4602, a relative measure of the enzyme activity in vivo and a reflection of the synthesis rate of 5-hydroxytryptamine (5-HT), was measured. The increase of 5-HTP was 30 times greater in the raphe nuclei (which contain serotonergic cell bodies) than the hippocampus or caudate (which contain serotonergic terminals). Pretreatment with chlorimipramine reduced the 5-HTP accumulation in the median but not dorsal raphe. The large amount of tryptophan hydroxylase in cell bodies appears to be active in vivo. The serotonin rapidly turning over there may have a functional role. 8 references. (Author abstract modified)

000169 Mendelson, Wallace B.; Hill, Shirley Y. NIMH, St. Elizabeths Hospital, Washington, DC 20032 **A dose-response study of the acute effects of ehtanol on the sleep of rats.** Bethesda, MD, NIMH, 1976. 1 p.

Dose/response data on the effects of ethanol on rat sleep are presented, including findings from administration of increasing doses (1.1, 1.5, 2.0, 2.5mg/kg) and equivolume saline intraperitoneally to five groups of six Ss. Injections were given 5 min before beginning of 7 hour recordings. Results indicate that percent rapid eye movement sleep decreased, while percent slow-wave sleep decreased. By dividing the recording into sequential 3.5hr periods, it became clear that this effect occurred most strongly in the first 3.5hrs of sleep. Although number of awakenings was not changed over the recording as a whole, they were significantly increased in the second half. This may reflect greatly decreased blood alcohol levels. Even the highest doses of ethanol did not produce prolongation of total sleep time in either the whole recording or the first or second halves. 1 reference.

000170 Meshali, Mahasen M.; Nightingale, Charles H. School of Pharmacy, University of Assuit, Assuit, Egypt **The effect of alpha-tocopherol deficiency on the pharmacokinetics and pharmacological effect of barbital.** Life Sciences (Oxford). 19(2):163-174, 1976.

The effect of alpha-tocopherol deficiency on barbital absorption, distribution, and elimination in rats was investigated. It was found that the in vitro transport of barbital through the everted intestine was more rapid in animals deficient in alpha-tocopherol as compared to controls. Pharmacokinetic analysis of blood level versus time data obtained on intact animals showed that the absorption rate constant was significantly increased and the elimination rate constant decreased in the vitamin deficient animals. The apparent volume of distribution was unchanged although the peak height and time of occurence of the blood level peak were different in the deficient animals. A correlation between pharmacokinetic and pharmacological data was found. The increased absorption and transport of barbital through the gastrointestinal membranes resulted in higher blood levels within a shorter period of time. The consequence of this phenomena is that the onset of sleep was shortened in animals with an alpha-tocopherol deficiency. It is concluded that tocopheral deficiency causes generalized changes in membrane structure, allowing alteration of pharmacokinetc and pharmacological effects of other drugs as well. 27 references. (Journal abstract modified)

000171 Minneman, Kenneth P.; Iversen, Leslie L. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Hills Road, Cambridge cb2 2OD, England **Enkephalin and opiate narcotics increase cyclic GMP accumulation in slices of rat neostriatum.** Nature (London). 262(5566):313-314, 1976.

The effects of morphine, levorphanol, dextrorphan, low enkephalin, and met-enkephalin on the accumulation of 3,5-adenosine monophosphate (cyclic AMP) and of cyclic 3,5-guanosine monophosphate (cyclic GMP) in rat neostriatum were studied in vitro. Morphine increases the accumulation of cyclic GMP and decreases the accumulation of cyclic AMP in rat striatal tissue slices. These actions are completely blocked by naloxone. Levorphanol mimics the actions of morphine on both cyclic nucleotides but dextrorphan does not. Neither low enkephalin not met-enkephalin affect cyclic GMP or cyclic AMP accumulation in the tissue slices; this lack of activity is attributed to the rapid inactivation of these compounds. In the presence of bacitracin, a peptidase inhibitor, both low enkephalin and met-enkephalin increase cyclic GMP accumulation and decrease cyclic AMP accumulation. It is suggested that the increase in cyclic GMP accumulation by both enkephalins and by morphine and other opiate narcotics may represent a mechanism by which the actions of these compounds are mediated at the cellular level. 13 references.

000172 Moleman, Peter; Bruinvels, Jacques. Department of Pharmacology, Erasmus University, P.O. Box 1738, Rotterdam, Netherlands **Differential effect of morphine on dopaminergic neurons in frontal cortex and striatum of the rat.** Life Sciences (Oxford). 19(8):1277-1282, 1976.

Experiments evaluate the effect of morphine on dopaminergic systems in the corpus striatum and in frontal parts of the cortex of rats after inhibition of the dopamine synthesis by alpha-methyl-para-tyrosine (alpha-MpT). Inhibition (by a single injection of 200mg/kg i.p.)was complete from 30 to at least 300 minutes after administration. When morphine (20mg/kg) was given intraperitonally 30 minutes after alpha-MpT treatment, an enhanced decline of dopamine was observed in frontal

parts of the cortex but not in the striatum. These results indicate that morphine affects dopaminergic neurons in frontal parts of the cortex differently from those in the striatum. It is suggested that may be caused either by a difference in the properties of dopaminergic nerve endings in both structures or by an effect of morphine on the input to the cortical system which is lacking in the striatum. 18 references. (Journal abstract modified)

000173 Moniuszko-Jakoniuk, Janina; Wisniewski, Konstanty. Zaklad Farmakologii AM, 15-222 Bialystok, Mickiewicza 2a, Poland **The influence of bradykinin and drugs blocking alpha and beta-adrenergic receptor on the stimulating effect of nialamide and L-DOPA.** Acta Physiologica Polonica (Warszawa). 27(4):395-399, 1976.

The influence of bradykinin on the central effects of Nialamide after administration of adrenergic blocking agents phentolamine and propranolol was studied in rats. It has been found that kinins increase psychostimulatory effects of Nialamide and L-DOPA as well as psychoinhibitory effects of propranolol without any changes in phentolamine action. Phentolamine and propranolol decrease stimulatory effects of Nialamide and L-DOPA only when they are given jointly with bradykinin. 8 references. (Author abstract modified)

000174 Moniuszko-Jakoniuk, Janina; Wisniewski, Konstanty; Koscielak, Maria. Department of Pharmacology, Medical School in Bialystok, Poland **Investigations of the mechanism of central action of kinins.** Psychopharmacology (Berlin). 50(2):181-186, 1976.

The effects of bradykinin and kallikrein on the levels of norepinephrine (NE), dopamine (DA) and serotonin (5-hydroxytryptamine, 5-HT) and of their metabolites normetanephrine, homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) in the cerebellum, corpus striatum, cortex, hippocampus, hypothalamus, medulla oblongata and midbrain were investigated in rats. The kinins decreased NE levels in corpus striatum, midbrain and cerebellum. They also decreased DA level in corpus striatum and increased the levels of 5-HT in corpus striatum and midbrain. Bradykinin decreased normetanephrine levels in corpus striatum, hippocampus and midbrain and the level of HVA in corpus striatum, and increased the levels of 5-HT in corpus striatum and hippocampus. It is concluded that kinins interact with neuromediators in the central nervous system. 25 references. (Author abstract modified)

000175 Montgomery, R. L.; Christian, E. L. Department of Anatomy, University of North Carolina at Chapel Hill, Chapel Hill, NC 27514 **Pathologic effects of antimetabolites on the hippocampus of diet controlled mice.** Brain Research Bulletin. 1(3):255-259, 1976.

Antimetabolites of nicotinamide and pyroxine (3-acetylpyridine and 4-methoxypyridoxine) are employed as analytical tools to attain the following objectives: 1) to induce acute histopathological changes in Spielmeyer's resistant sector H2; and 2) to determine if diets free of niacin or pyroxine influence hippocampal neurons in mice treated with antimetabolites. Marked histological changes are observed in the hippocampi of mice maintained on niacin diets following a single injection of 3-acetylpyridine. Extensive neuronal damage occurs in areas H2, H3, and to a lesser degree in the dentate gyrus. The neurons appear to be shrunken, and deeply basophilic, and exhibit a loss of intracellular architecture. The neuronal response in pyridoxine deficient mice treated with 4-methoxypyridoxine is not considered to be unusual. 13 references. (Author abstract modified)

000176 Morgan, William W.; Reiter, Russel J.; Pfeil, Karla A. Dept. of Anatomy, University of Texas Health Science Center, San Antonio, TX 78284 **Hamster pineal noradrenaline: levels over a regulated lighting period and the influence of superior cervical ganglionectomy.** Life Sciences (Oxford). 19(3):437-440, 1976.

A recently developed, highly sensitive enzymatic isotopic method was used to measure noradrenaline (NA) levels in the pineal of golden hamsters, Mesocricetus auratus, that were subjected to regulated lighting periods and some were also bilaterally superior cervical gangliocectomized (SCGX). The results show conclusively that, unlike the rat, there is no significant daily variation in NA content in the pineal of male hamsters. Bilateral SCGX caused the complete depletion of NA in the hamster pineal. As in the rat pineal, these results indicate that NA in the hamster pineal is localized almost exclusively in sympathetic nerve endings whose cell bodies are located in the superior cervical ganglion. Further areas of research are indicated. 13 references. (Author abstract modified)

000177 Mostafa, M.-H.; Rakonczay, Z. Institute of Biochemistry, Biological Research Center, Hungarian Academy of Sciences, Szeged, Hungary **Effect of chlorpromazine on tyrosine hydroxylase in rat brain striatum and beef adrenal medulla.** Agressologie (Paris). 17(2):81-86, 1976.

The effect of chlorpromazine and chlorpromazine free radical on tyrosine hydroxylase was studied. In the first experiment, male PVG/C rats weighing 150-200g were given 5 or 20mg/kg i.p. of chlorpromazine for 4-12 days at 24 hr intervals, while controls received 0.9% NaCl i.p. Two hours after the last injection, the animals were decapitated, and their brains were removed. The striatum was dissected, homogenized, and centrifuged, and tyrosine hydroxylase was measured in the resulting supernatant. Bovine adrenal glands were removed from the animal within 2 hrs after killing, homogenized and centrifuged, tyrosine hydroxylase was measured in the supernatant. The enzyme assay is described. Chlorpromazine, and both chlorpromazine and chlorpromazine free radical had a greater inhibitory effect on striatal tyrosine hydroxylase than on bovine adrenal tyrosine hydroxylase. The kinetics of the enzyme inhibition are discussed. Chronic pretreatment with chlorpromazine for 10-12 days causes an increase in striatal tyrosine hydroxylase activity. 35 references.

000178 Mrongovius, Robert I. Raymond Purves Research Laboratories, North Shore Hospital of Sydney, St. Leonards, N.S.W. Australia 2065 **Structure-activity correlations for central depressant acylureas and alkylureas.** European Journal of Medicinal Chemistry (Paris). 10(5):474-479, 1975.

The structure/activity correlations for central depressant acylurans and alkylureas were examined. The central depressant activity of homologous acylureas has a parabolic dependence on lipophilicity: the depressant activity is maximal for acylureas of 7 acyl carbons. Among isomeric acylureas activity increases with branching of the alkyl chain. The central depressant potencies of alkylureas are dependent on lipophilic, polar and x-hydrogen effects and branching of the alkyl chain results in loss of activity. Depressant activity on the central nervous system was assessed using the inclined screen test. Structure activity correlations were obtained by aa Hansch analysis. 33 references. (Author abstract modified)

000179 Mukherjee, B. P.; Bailey, Paul T.; Pradhan, S. N. Department of Pharmacology, College of Medicine, Howard University, Washington, DC 20059 **Temporal and regional dif-**

ferences in brain concentrations of lithium in rats. Psychopharmacology (Berlin). 48(1):119-121, 1976.

The time course of lithium (Li) concentrations in different brain areas and in peripheral tissues, was investigated in the rat for a comparison with other research data. Li concentrations have been estimated in several peripheral tissues (serum, heart, kidney, liver and skeletal muscle) and different brain areas (cortex, caudate nucleus, hypothalamus, diencephalon, midbrain, pons-medulla and cerebellum) at different intervals (0.5to 48 h) after administrations of 3mEq/kg of lithium chloride (LiC). The Li concentrations in the brain areas increased gradually, reaching their peak at 8 h; the hypothalamus showed the highest concentration measured between 0.5and 8 h; after 8 h the highest concentration was observed in the caudate nucleus, followed approximately by those of the cortex, rest of the diencephalon, and other areas. Concentration of Li in the skeletal muscle, although initially less, was maintained at a higher percentage of the initial level for more than 24 h compared to the other peripherlal issues. 13 references. (Author abstract modified)

000180 Muramatsu, Makoto; Kuriyama, Kinya. Department of Pharmacology, Kyoto Prefectural University of Medicine, Kamikyo-ku, Kyoto 602, Japan **Effect of organophosphorus compounds on acetylcholine synthesis in brain.** Japanese Journal of Pharmacology (Kyoto). 26(2):249-254, 1976.

The effects of parathion and di-isopropyl fluorophosphate (DFP) on acetylcholine (ACh) synthesis in the mouse brain were investigated. In addition to cholinesterase (ChE) inhibition, parathion showed inhibitory effects on the activity of synaptosomal choline acetyltransferase (ChAc), and on the uptake of radiolabeled methylcholine and ACh synthesis in subcellular fractions of the brain. DFP inhibited ChE activity, but had no significant effects on the choline uptake and ACh synthesis. Possible significance of these findings in the pharmacological actions of organophosphorus compounds is briefly discussed. 15 references.

000181 Myers, R. D.; Simpson, C. W.; Higgins, Diane; Nattermann, R. A.; Rice, J. C.; Redgrave, P.; Metcalf, G. Department of Psychological Sciences, Purdue University, Lafayette, IN 47906 **Hypothalamic Na+ and Ca++ ions and temperature set-point: new mechanisms of action of a central or peripheral thermal challenge and intrahypothalamic 5-HT, NE, PGE1 and pyrogen.** Brain Research Bulletin. 1(3):301-327, 1976.

The effects of changes in ambient and central temperature amines, PGE1 and pyrogen were investigated with respect to the mechanism of Na+ to Ca++ ratio in the posterior hypothalamus of the unrestrained cat. The results suggest that if the Na+ to Ca++ ratio in the posterior hypothalamus stablishes and maintains the set point for body temperature of 37 degrees to 38 degrees C, the mechanism of lability of Ca++ through changes in binding characteristics, transport, or metabolism of the Ca+ ion serves two purposes: 1) the active defense of the set-point temperature through gradations in ion shifts, and 2) the upward or downward change in set-point value, pathological or normal, triggered by virtue of impulses from the anterior hypothalamus. 83 references. (Author abstract modified)

000182 Nagayama, Haruo; Takagi, Akinori; Tateishi, Tadaaki; Takahashi, Ryo. Department of Neuropsychiatry, Negasaki University Medical School, Japan **Studies on the situational factors affecting the effect of psychotropic drugs -- I. Daily fluctuation of sedative effect of tetrabenazine.** Psychiatria et Neurologia Japonica (Tokyo). 77(12):925-932, 1975.

In order to test some situational effects on the effectiveness of psychotropic drugs, tetrabenazine (similar in effects to short-term administration of reserpine) was given to rats with the dosage time varied. Dosage was 50 mg/kilogram bodyweight. It was given both in the daytime from 7:30 through 19:30 and at night, from 19:30 to 7:30. The lasting effects of the sedative showed a significant difference according to the time of dosage. Administration at 10:30 produced longest-lasting effects, 1490 minutes, while administration at 7:30 produced the lowest effect length of 736 minutes. Similar results were gained from lower dosages of 10mg/kilogram. Reasons for these differences in effect were probably due to the synthesis rates of serotonin within the brain. 23 references.

000183 Nahorski, S. R.; Pratt, C. N. F. W.; Rogers, K. J. Department of Pharmacology, University of Sheffield, England **Increased cerebral cyclic GMP concentration induced by muscarinic cholinergic agonists and prostaglandin F2alpha.** British Journal of Pharmacology (Basingstoke). 57(3):445P-446P, 1976.

The effects of several compounds on cerebral cyclic GMP formation was studied after injection into the right jugular vein of a neonate chick. Administration of oxotremorine, arecoline or methacholine induces a rapid increase in cyclic GMP concentration. Prostaglandin F2-alpha also increases the nucleotide concentration in vivo. Noradrenaline, dopamine, 5-hydroxytryptamine, adrenaline, isoprenaline, clonidine, histamine, gamma-aminobutyric acid and prostaglandin E1 are ineffective in increasing cyclic GMP concentration, even in doses up to those producing marked behavioral effects. In vitro studies utilizing slices of chick cerebral hemisphers were performed in which the effects of muscarinic agonists were determined. In the presence of the potent phosphodiesterase inhibitor papaverine, the concentration of cyclic GMP is twice as high as in its absence. Exposure to oxotremorine produces a further 100% increase in cyclic GMP only in the presence of papaverine. It is concluded that the factors regulating cerebral cyclic GMP concentration differ from those controlling cyclic AMP. In chick cerebral tissue, muscarinic agonists and prostaglandin F2-alpha stimulate cyclic GMP formation, but whether or not these effects result from the direct stimulation of cell surface receptors remains to be established. 6 references.

000184 Nakamura, Keiji; Nakamura, Kazuo. Department of Pharmacology, Nippon Roche Research Center, Kamakura 247, Japan **Behavioral and neurochemical changes following administration of 6-hydroxydopamine into the ventral tegmental area of the midbrain.** Japanese Journal of Pharmacology (Kyoto). 26(2):269-273, 1976.

The effects of destruction of the ventral tegmental areas of the rat brain by 6-hydroxydopamine on gross behavior, action of d-methamphetamine, action of apomorphine, interaction of chlorpromazine with d-methamphetamine or apomorphine, and on neurochemical activity in the brain were examined. A direct administration of 6-OHDA into the ventral tegmental A-10 cells area caused aggressive behavior and locomotor activation accompanied with a marked decrease in 5-hydroxyindoleacetic acid contents in all of cerebral regions but there was no effect on dopamine and dihydroxyphenylacetic-acid contents in the mesolimbic olfactory tubercle. Neurochemical determination is thus considered a prerequisite for functional analysis after the 6-OHDA administration into the discrete cerebral regions.

000185 Nakano, Takasuke; Taira, Norio. Department of Pharmacology, Tohoku University School of Medicine, Sendai,

Japan **5-hydroxytryptamine as a sensitizer of somatic nociceptors for painkproducing substances.** European Journal of Pharmacology (Amsterdam). 38(1):23-29, 1976.

Because sensitization by 5-hydroxytryptamine (5-HT) of pain receptors has been found to be extremely marked in the vein, experiments to determine whether 5-HT would sensitize somatic nociceptors in animals were conducted with vocalization of conscious dogs as a measure of nociception. The experiments clearly demonstrated that 5-HT administered into the femoral artery lowered the threshold for vocalization as a response of conscious dogs to acetylcholine (ACh) and bradykinin injected into the same artery. Doses of 5-HT required to sensitize the somatic nociceptors were relatively large. Therefore, it may not be relevant to relate the present results directly to implication of 5-HT in pathological pain occurring in occlusive vascular disease in which 5-HT is probably released from aggregated platelets. 8 references. (Author abstract modified)

000186 Naumenko, Eugene V.; Serova, Lidia I. Institute of Cytology and Genetics, Siberian Branch of the Academy of Sciences of the U.S.S.R., Novosibirsk, Russia **Diencephalic dopamine receptors and regulation of pituitary-testicular system.** Brain Research (Amsterdam). 110(3):537-545, 1976.

An examination of the role of brain dopamine receptors in the regulation of the hypothalamic/pituitary/testicular complex is conducted with special attention given to the search for their localization in the medial basal hypothalamus (MBH) and other regions of the diencephalon. Injection of dopamine, DOPA or apomorphine into the third brain ventricle resulted in an increase in the plasma testosterone level. Pimozide, blocking dopamine receptors, as well as complete, long posterior and posterior but not anterior deafferentation of the MBH abolished the stimulating action of dopamine. After direct injection of dopamine into the arcuate nucleus there was no stimulating effect on the pituitary/gonadal system. At the same time, local injections of dopamine and apomorphine into the medial part of the subthalamus or periventricular gray matter of the caudal thalamus were followed by a distinct increase in the plasma testosterone level. The conclusion is drawn that the brain dopaminergic neurons activating the pituitary/gonadal system in the male are localized outside the hypophyseotrophic area of hypothalamus in zona incerta and caudal part of the thalamus. After stimulation of diencephalic dopamine receptors, nerve impulses are transmitted to the MBH through the posterior hypothalamic pathways. 28 references.

000187 Ng, R. H.; Marshall, F. D. Department of Biochemistry, University of South Dakota School of Medicine, Vermillion, SD 57069 **The effects of various agents in vitro on homocarnosine-carnosine synthetase from rat brain.** Experientia (Basel). 32(7):839-841, 1976.

The first evidence that homocarnosine/carnosine synthetase from rat brain requires free sulfhydryl groups for activity is presented. The activity of the synthetase can be stabilized by dithioerythritol and inhibited strongly by Cu2 plus, Cd2 plus, HG2 plus, and Zn2 plus. It can be inhibited to a lesser extent by Ca2 plus, Ni2 plus, Li, and the central nervous system agents, chlorpromazine, alpha-methyl DOPA, and norepinephrine at the concentrations which were tested. Findings have implications for further studies of the unique role of the two depeptides in the central nervous system. 12 references. (Author abstract modified)

000188 Oka, Tetsuo; Hosoya, Eikichi Department of Pharmacology, School of Medicine, Tokai University, Isehara, Kanagawa, Japan **Effects of humoral modulators and naloxone on morphine-induced changes in the spontaneous locomotor activity of the rat.** Psychopharmacology (Berlin). 47(3):243-248, 1976

A study was carried out to determine the effects of neurohumoral transmitters and of naloxone on morphine induced depression and stimulation of spontaneous locomotor activity (SLMA) in nontolerant rats. Subcutaneous (sc) injection of 20mg/kg of morphine HCl decreases SLMA; this effect is significantly antagonized by para-chlorophenylatanine (p-CPA). When rats pretreated with p-CPA are given 5-hydroxytryptophan (5-HT) before morphine injection, the marked sedative response to morphine is restored. A significant increase in SLMA is produced by 5mg/kg morphine HCl sc. The magnitude of the increase is reduced by atropine, scopolamine or alpha-methyl-para-tyrosine. Both the increase in SLMA by 5mg/kg morphine and the decrease in SLMA produced by 20mg/kg morphine are completely antagonized by sc injection of naloxone. It is suggested that: 1) the morphine induced decrease in SLMA of rats may depend on the release of 5-HT by morphine; 2) adrenergic mechanisms and cholinergic mechanisms both participate in morphine induced increases in SLMA; and 3) the receptor with which morphine interacts to produce stimulation is chemically identical with or very similar to the receptor with which morphine combines to induce depression although the former receptors are likely to be located on different neurons from the latter. 38 references. (Author abstract modified)

000189 Olesen, O. Vendelin; Jensen, Jorgen; Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus Univ. Institute of Psychiatry, DK-8240 Risskov, Denmark **Effect of potassium on lithium-induced growth retardation and polyuria in rats.** Acta Pharmacologia et Toxicologia (Kobenhavn). 36(2):161-171, 1975.

The effect of potassium on lithium induced growth retardation and polyuria was examined in rats given food containing 100mmol/kg of lithium and 600mmol/kg of sodium. The increase of the potassium content of the food from 100mmol/kg to 700mmol/kg led to a statistically significant increase of the weight gain and diminished the polyuria with unaltered serum lithium concentration; in control rats the high electrolyte content had a slightly decreasing effect on normal weight gain. At 9 weeks the lithium treated rats and the control rats weighed almost the same. At a lower level of sodium in the food (350mmol/kg) addition of extra potassium had no effect on the weight gain of the rats given lithium, but the polyuria was reduced to the same level as that in the experiment with the high sodium diet. Addition of sodium to the food in place of potassium also led to increased weight gain and diminished polyuria, but the effect of sodium was less than the effect of potassium and could be accounted for by a sodium induced lowering of the serum lithium concentration. Lithium administration led to a shift of the urine pH in an alkaline direction; this effect was counteracted by potassium in all 3 experiments. It is concluded that potassium counteracts lithium induced growth retardation and polyuria in rats; the effects are not mediated via a reduction of the serum lithium concentration. 7 references. (Author abstract)

000190 Pachecka, J.; Salmona, M.; Cantoni, L.; Mussini, E.; Pantarotto, C.; Frigerio, A.; Belvedere, G. Medical Academy, Banacha 1, Warsaw, Poland **Activity of liver microsomal monooxygenases on some epoxide-forming tricyclic drugs. I. Kinetics in vitro.** Xenobiotica (London). 6(10):593-598, 1976.

The monooxygenase activity that forms epoxides was studied in rat liver microsomes using as substrates carbamazepine and cyclobenzaprine, tricyclic drugs that form stable compounds in vivo and in vitro. A simple gas chromatographic method was used to determine the amount of epoxide formed, and the linearity of the enzymic reaction with time and protein concentration was demonstrated. Pretreatment with carbamazepine was shown to increase the rate of formation of carbamazepine epoxide in rate liver microsomal preparations. A study of the effect of SKF-525-A on the formation of these epoxides is also summarized. 12 references. (Author abstract modified)

000191 Patrick, Timothy B.; Bresee, Randall R. Department of Chemistry, Southern Illinois University, Edwardsville, IL 62026 **Enthalpies of hydrogen bonding in psychotropic drugs.** Journal of Pharmaceutical Sciences. 65(7):1066-1067, 1976.

The enthalpy of hydrogen bonding with phenol and some antidepressant, anticonvulsant and antianxiety agents (promazine, amitryptyline, imipramine, chlorpromazine, diazepam, phenobarbital, dimethadione, phenytoin and bemegride) was determined via IR spectroscopic measurements and NMR spectroscopic measurements in order to confirm the theory that hydrogen bond acceptance is not responsible for variations in anticonvulsant activity. Hydrogen bonding enthalpies for anticonvulsants measured by IR spectroscopy have a value of about 0.4kcal/mole; enthalpies measured by NMR spectroscopy have a value of about 4.6kcal/mole. The antipsychotic drugs and antidepressant drugs have enthalpy values that are 1.41kcal/mole (IR) and 2.77kcal/mole (NMR) higher than those of anticonvulsants. Diazepam, which has both tranquilizing and anticonvulsants activities, has enthalpy of hydrogen bonding intermediate between those of the two classes of drugs. It is suggested that hydrogen bond acceptance alone is not responsible for the differences in activity within the drug classes studied. 9 references.

000192 Pelton, E. Williams, II; Chase, Thomas N. Laboratory of Clinical Science, NIMH, Bethesda, MD **L-dopa and the treatment of extrapyramidal disease.** Advances in Pharmacology and Chemotherapy. 13:253-304, 1975.

In a continuing series of reports on advances in pharmacology and chemotherapy, the literature on L-dopa and the treatment of extrapyramidal disease is reviewed. The principal focus of the review is on the function of central dopamine containing neural systems in view of their crucial role in mediating the effects of L-dopa on motor behavior. The areas covered are: metabolism; pharmacology; and therapeutic applications. The fortuitous circumstances which contribute to the ability of L-dopa to improve Parkinsonian signs are discussed. 351 references.

000193 Pennings, Ed J. M.; Vrielink, Rein; Van Kempen, Godfried M. J. Biochemical Laboratory, Mental Hospital Endegeest, Degstgeest, The Netherlands **Anomalous effect of probenecid on rat brain phenolsulphotransferase.** Biochemical Pharmacology (Oxford). 25(14):1687-1690, 1976.

The effect of probenecid on the enzyme phenolsulphotransferase, which catalyzes the conversion of 3-methoxy-4-hydroxyphenylethylene-glycol (MHPG) to MHPG-sulfate, was studied using enzyme prepared from rat brain. At the optimal concentration of substrate, 0.2mM, addition of 1.0mM of probenecid or 2.0mM of probenecid produces a significant increase in the amount of formed product. Addition of 5mM of probenecid produces a decrease in the amount of formed product. At concentrations of substrate lower than 0.2mM, addition of probenecid results in inhibition of activity, while addition of probenecid to 0.5mM of substrate increase activity. Probenecid appears to possess both an inhibitory and an activating action on rat brain phenolsulphotransferase, depending on its own concentration and on that of the substrate. In rat liver enzyme preparations, probenecid produces only a concentration dependent inhibitory action. The effect of the drug cannot be ascribed to an action on intact membrane structures. The extent to which these effects influence the MHPG-sulfate concentration in brain after probenecid administration in vivo cannot be anticipated. In view of the high doses of probenecid administered to patients and animals, these findings may have practical implications with regard to the measurement of MHPG-sulfate after probenecid treatment and they may complicate the interpretation of the results of in vivo experiments using the drug. 6 references.

000194 Perez, Vernon J.; Olney, John W.; Frolichstein, Constance F.; Martin, Julie F.; Cannon, William O. Dept. of Biochemistry, Texas Tech. University Medical School, Lubbock, TX 79404 **Regional uptake of neurotoxic and nontoxic amino acids in vivo by the infant mouse brain.** Biochemical Pharmacology (Oxford). 25(12):1415-1419, 1976.

The acidic amino acids, glutamate, cysteate and homocysteate, destroy neurons in the arcuate nucleus of the hypothalamus when administered subcutaneously to infant mice, but alanine, a neutral amino acid, does not. The neurotoxicity of glutamate, cysteate and homocysteate was confirmed in this study. It was further demonstrated that glutamate accumulates in the arcuate nucleus after the administration of glutamate but not after cysteate or homocysteate administration. This rules out the possibility that the neurotoxicity of the latter two compounds is mediated by the conversion in vivo of these compounds to glutamate. It supports the thesis that the similar neurotoxic manifestations of these compounds stem from the similar molecular structure they share. Alanine accumulated in the arcuate and ventromedial nuclei of the hypothalamus and, to a lesser extent, the medial nucleus of the thalamus, but had no neuropathologic effects in any brain region. The failure of alanine to damage arcuate neurons is interpreted as evidence that, because of its dissimilar molecular structure, it either does not react or reacts very differently from the acidic neurotoxic amino acids at some receptor locus on neural membranes. 28 references. (Author abstract)

000195 Peringer, E.; Jenner, P.; Donaldson, I. M.; Marsden, C. D.; Miller, R. Wellcome Research Laboratories, Langley Court, Beckenham, Kent BR3 3BS, England **Metoclopramide and dopamine receptor blockade.** Neuropharmacology (Oxford). 15(8):463-469, 1976.

The effect of metoclopramide administration on turnover of brain dopamine and the manner in which the changes are mediated were studied in mice. Metoclopramide produced a dose dependent increase in striatal homovanillic acid (HVA) and mesolimbic concentration. Dihydroxyphenylacetic acid levels were only elevated at high dosage levels. Metoclopramide accelerated cerebral dopamine disappearance following pretreatment with alphamethyl para tyrosine and caused an increased accumulation of whole brain dihydroxyphenylalanine (DOPA) following pretreatment with NSD 1034. It is suggested that metoclopramide blocks cerebral dopamine receptors causing increased turnover of dopamine. Chronic administration of metoclopramide produced a reduction in its effect on HVA levels as was observed following chronic haloperidol treatment. Metoclopramide had no effect on the in vitro dopamine stimulated adenylate cyclase system of the rat striatum. Uni-

lateral striatal injection of metoclopramide produced ipsiversive turning behavior in response to systemically administered apomorphine, indicating a direct mode of action. It is suggested that metoclopramide causes a blockade of dopamine receptors by a mechanism differing from that of classical neuroleptics. 58 references. (Author abstract modified)

000196 Perry, Thomas L.; MacLean, Janet; Perry, Thomas L., Jr.; Hansen, Shirley. Department of Pharmacology, University of British Columbia, Vancouver V6T 1W5, Canada **Effects of 3-acetylpyridine on putative neurotransmitter amino acids in rat cerebellum.** Brain Research (Amsterdam). No.109:632-635, 1976.

Amino compounds in the protein free extracts of individual rat cerrebella were quantitated on an automatic amino acid analyzer to determine the effect of 3-acetylpyridine (3-AP). The technique allows accurate measurement of about 35 amino acids and related compounds. The 10 most abundant amino compounds are: taurine, phosphoethanolamine, aspartic acid, total glutathione (as GSH), threonine, serine, glutamic acid, glutamine, glycine and gamma-aminobutyric acid (GABA). Of these, aspartate and glutamate are putative excitatory neurotransmitters, and taurine, glycine and GABA are putative inhibitory neurotransmitters. Slight reductions occurred in the mean contents of aspartate and glutamate in the cerebella of the 3-AP treated rats, which does support the theory that either compound is a natural excitatory transmitter of the climbing fibers. The only important change in amino acids in rat cerebellum produced by 3-AP was a highly significant reduction in taurine content, more marked after multiple injections. 11 references.

000197 Peterfy, G.; Pinter, E. J.; Pattee, C. J. Allan Memorial Institute of Psychiatry, Royal Victoria Hospital, Montreal, Canada **Psychosomatic aspects of catecholamine depletion: comparative studies of metabolic, endocrine and affective changes.** Psychoneuroendocrinology (Oxford). 1(3):243-253, 1976.

An acute depletion of catecholamines was brought about in healthy volunteers to study the resultant metabolic, endocrine and affective changes. Fifteen subjects were reserpinized using large parenteral doses (5 mg i.m. every 8 hr/48 hr); in nine of these, the effects of a sympathomimetic compound (methamphetamine, i.v. 0.2mg/kg/15 min) were also studied at the end of 48 hr of reserpine treatment. The following biochemical determinations were made: plasma free fatty acids (FFA), blood glucose, plasma corticoids. Affective functions were assessed using the Clyde Mood Scale (mood changes) and the Gleser-Gottschalk method of verbal samples (anxiety, inward/outward hostility). A substantial, significant increase of FFA production occurred within 12 hr of reserpinization and persisted throughout the 48 hr experimental period. Circulating corticoids rose significantly and maintained a high level during the same period; blood glucose showed no meaningful change. The sympathomimetic compound (methamphetamine) led to significant stimulation of both FFA and corticoids; reserpinization partially inhibited its effect on FFA and completely abolished the rise of corticoids on administration of methamphetamine after reserpine. Reserpinization induced a progessive, marked influence on affect; depression, increased anxiety, hostility and even suicidal tendencies were observed. In 80% of the subjects, administration of methamphetamine in the reserpinized state elicited a fast developing, transient, delirium like state with initial rapid euphoria and distortion of reality perception. This degree of eupho ria, quickly merging into delirium, did not occur with methamphetamine given under basal conditions. These observations lend further support to the role of endogenous catecholamines in maintaining emotional stability and possibly protecting the brain in states of grossly distorted metabolic and humoral balance. 24 references. (Author abstract modified)

000198 Peterson, Dale W.; Sparber, Sheldon B. Department of Pharmacology, University of Otago, Medical School, Dunedin, New Zealnad **Differential actions of d- and l-amphetamine on the metabolism of 3H-norepinephrine in rat brain.** Pharmacology Biochemistry and Behavior. 4(5):545-549, 1976.

Approximately equieffective doses of d-amphetamine and l-amphetamine, using suppression of operant fixed-ratio responding for food reinforcement as the determinant of potency, were compared for their ability to alter the disposition of the major and minor metabolites of radiolabelled norepinephrine (NE) in push/pull perfusates from rat brain lateral vetricle. While 3mg d-amphetamine/kg and 6mg l-amphetamine/kg both increase total (3H) and the relative amounts of the minor metabolites 3H-normetanephrine and 3H-dihydroxymandelic acid, only l-amphetamine causes a significant increase in the major 3H-NE metabolite, methoxyhydroxyphenylethyleneglycol (MHPG). The data is discussed in relation to the abilities of the isomers of amphetamine to stereoselectively interact with noradrenergic neurons at doses that produce similar effects upon operant behavior. It is suggested that l-amphetamine effects noradrenergic function to a greater extent tha n does d-amphetamine in doses producing comparable behavioral effects. 38 references. (Author abstract modified)

000199 Peterson, Neal A.; Raghupathy, E.; Estey, S. J. Brain-Behavior Research Center (Langley-Porter Neuropsychiatric Institute, Univ. of Calif.), Sonoma State Hospital, Eldridge, CA 95431 **Effects of vinca alkaloids on uptakes of amino acids by rat brain synaptosomes.** Biochemical Pharmacology (Oxford). 25(12):1389-1395, 1976.

Rat brain synaptosomes were studied for the effects of vinca alkaloids on uptakes of amino acids. Synaptosomal uptakes of a number of amino acids were strongly inhibited by vinblastine (I50=30uM-50uM). Vincristine was a less effective inhibitor and colchicine had virtually no effect. The inhibitory effects of vinblastine on uptakes of alanine, leucine and serine were modified by cations and nucleotides. The degree of inhibition was reduced by cations of magnesium, calcium, and sodium; nucleotides antagonized the inhibitory effects of vinblastine but this effect required the presence of divalent cations. The inhibitory effects of vinblastine were almost abolished when the incubations were carried out at 5 degrees instead of 37 degrees. The efflux of amino acids from synaptosomal particles was retarded by vinblastine; this effect could be observed at a concentration as low as 15uM. By analogy with the effects of vinca alkaloids on biological processes in other tissues, the present results suggest the neurotubular protein participates in the initial rapid uptake and the subsequent efflux of amino acids in synaptosomal fractions. 22 references. (Author abstract modified)

000200 Phillips, Anthony G.; Carter, David A.; Fibiger, Hans C. Department of Psychology, University of British Columbia, Vancouver, B.C., Canada **Decreased intracranial self-stimulation after neuroleptics or destruction of the nigroneostriatal bundle: performance or reinforcement deficit?** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 272-280).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium in April 1975, the catecholamine (CA) hypothesis of reward, which relies greatly on psychopharmaceutical data and the neuroanatomical correlation between intracranial self-stimulation (ICSS) sites and the ascending CA systems as revealed by histochemical fluorescence, is discussed. The role of dopamine (DA) reward is examined by questioning the interpretation of the disruptive effects of neuroleptics on ICSS and by analyzing the results of recent lesion studies which provide some evidence for the mediation of reward by dopaminergic systems. Specific data are presented on the disruption of operant responding for ICSS and food following DA receptor blockade and on the disruption of ICSS in the nigroneostriatal bundle (NSB) after unilateral 6-hydroxydopamine (6-OHDA) lesions of the substantia nigra. Overall findings indicate that dopaminergic NSB plays an important role in operant responding. It is suggested that because lesions of this projection produce substantial deficits in motor tasks, experiments which merely demonstrate an effect on bar-pressing for ICSS after pharmacological or surgical interruption of this system do not necessarily implicate this projection in reward or reinforcement mechanisms. By using unilateral lesions, however, evidence shows that the dopaminergic NSB is a neural substrate for both reward and motor functions. 27 references.

000201 Phillips, K. G.; Lowe, G. Department of Psychology, University of Hull, Hull, England **Cholinergic modification of drug-induced stereotypy in rats.** Bulletin of the British Psychological Society (London). 28:249, 1975.

The possibility of cholinergic modification of drug induced stereotypy in rats was investigated to determine its relevance for psychosis research. Such stereotyped behavior in animals has been proposed as a model of endogenous psychoses and is believed mediated by dopamine. Baseline levels of stereotyped behavior induced in rats by d-amphetamine were potentiated by the anticholinergic atropine and antagonized by the cholinomimetic physostigmine. Noncentrally acting methylatropine and neostigmine were ineffective in this respect. These findings are consistent with the hypothesis that cholinergic activity balances the dopaminergic mediation of stereotyped behavior. The implications for psychosis research are discussed. 3 references. (Author abstract)

000202 Placheta, P.; Singer, E.; Kriwanek, W.; Hertting, G. Institute of Pharmacology, University of Vienna, Wahringer Strasse 13a, A-1090 Vienna, Austria **Mepiprazole, a new psychotropic drug: effects on uptake and retention of monoamines in rat brain synaptosomes.** Psychopharmacology (Berlin). 48(3):295-301, 1976.

The effects of mepiprazole (EMD 16923) on the uptake of radiolabeled norepinephrine (NE), radiolabeled dopamine (DA), and radiolabeled serotonin (5-HT) into rat brain synaptosomes from cerebral cortex, corpus striatum, and hypothalamus were investigated in vitro. Several psychotropic drugs including oxypertine, dextroamphetamine, imipramine, desipramine, chlorimipramine, amitriptylene, and chlorpromazine were tested for comparison. Mepiprazole was a relatively weak inhibitor of monoamine uptake and exhibited its strongest action on hypothalamic 5-HT uptake, being almost as potent as disipramine. The influence of the drugs on the retention of radiolabeled amines previously taken up by whole brain synaptosomes was also studied. Unlike the tricyclic antidepressants, mepiprazole, dextroamphetamine and oxypertine markedly increased in the efflux of radioactivity from the synaptosomes. The ability of mepiprazole to increase 5-HT concentration at the receptor level by a combination of neuronal uptake inhibition and release is discussed in relationship to the contral actions of the drug. 34 references. (Author abstract modified)

000203 Plotnikoff, Nicholas P.; Kastin, Abba J.; Coy, David H.; Christensen, Carl W.; Schally, Andrew V.; Spirtes, Morris A. Veterans Administration Hospital, New Orleans, LA 70146 **Neuropharmacological actions of enkephalin after systematic administration.** Life Sciences (Oxford). 19(8):1283-1288, 1976.

A study found that a pentapeptide, methionine-enkephalin, which interacts with opiate receptors in the brain, markedly potentiates the behavioral effects of DOPA when administered intraperitoneally into mice. These effects, which were even more striking with D-alanine-2-methionine-5-enkephalin but less with morphine, persisted at least 2 hours after systematic injection of the peptide. Only a weak effect of enkephalin was seen in a serotonin potentiation test. Systematic injections of enkephalin resulted in a significant reduction of footshock induced fighting and slight reduction in audiogenic seizures in mice. The results suggest that the CNS effects observed after systematic administration of enkephalin may involve the dopaminergic receptor mechanism. 23 references. (Journal abstract)

000204 Pradhan, S. N. Howard University College of Medicine, Department of Pharmacology, Washington, DC 20001 **Balance of central neurotransmitter actions in self-stimulation behavior.** In: Waquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 171-185).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium, in April 1975, the roles of putative central neurotransmitters, such as norepinephrine (NE), dopamine (DA), acetylcholine (ACh), 5-hydroxytryptamine (serotonin or 5-HT), and histamine in intracranial self-stimulation (ICSS) are discussed. Neuropharmacological data are reviewed which indicate that drugs which alter concentration of a neurotransmitter at the respective central receptor sites by affecting its synthesis, storage, release, action, reentry, or disposal also modify ICSS responding. These data suggest that ACh and 5-HT appear to inhibit such responding. It is not clear whether NE or DA, or both, are involved in facilitation of this behavior. It is suggested that both DA and NE may function in a concerted manner. Neurochemical, neuroanatomical, and neuropharmacological research also indicates that during drug induced ICSS, more than one neurotransmitter system is stimulated. Overall findings suggest: 1) a concept of balance among the central neurotransmitters; 2) that changes in the activity of one may initiate changes in others through involvement of common enzymatic or other neurophysiological mechanisms; and 3) that the organism's reward system is operationally integrated with related functional systems and multitransmitter balance. 80 references.

000205 Pugsley, T. A.; Lippmann, W. no address **Effects of pyrroxan and chlordiazepoxide on biogenic amine metabolism in the rat brain.** Psychopharmacology (Berlin). 50(2):113-118, 1976.

The effects of pyrroxan on catecholamine turnover and serotonin (5-hydroxytryptamine, 5-HT) turnover in the rat brain were studied and compared with those of chlordiazepoxide. Pyrroxan increased brain norepinephrine (NE) turnover; chlordiazepoxide did not alter NE turnover. Pyrroxan did not affect overall dopamine (DA) turnover but it appeared to accelerate DA turnover initially; chlordiazapoxide decreased DA

turnover. Both drugs decreased 5-HT turnover without significant monoamine oxidase activity or blockade of the 5-HT reuptake mechanism. Both drug produced significantly elevated levels of radiolabeled 5-HT after intraventricular injections of radiolabeled 5-HT as compared with controls. Neither drug causes consistent changes in endogenous 5-HT, 5-hydroxyindoleacetic acid or tryptophan levels. Neither drug potentiated the behavioral effects of L-Dopa nor increased the 5-hydroxytryptophan behavioral syndrome in the mouse. It is suggested that pyrroxan may be expected to exhibit a spectrum of activity between that of minor tranquilizers and major tranquilizers, characterized by antianxiety action together with sedative or tranquilizing activity. 44 references. (Author abstract modified)

000206 Quartey, Gilbert R. C.; Johnston, Jane Anne; Rozdilsky, Bohdan. Department of Neurosurgery, University of Saskatchewan College of Medicine, Saskatoon, Saskatchewan, S7N OW8 Canada **Decadron in the treatment of cerebral abscess: an experimental study.** Journal of Neurosurgery. 45(3):301-310, 1976.

Forty rabbits were inoculated with streptococcus pyogenes or staphylococcus aureus to produce cerebral abscesses. In the control group, an abscess at the stage of granulation tissue encapsulation containing the inoculated organisms was found. The surrounding brain showed a marked inflammatory response. In the decadron plus antibiotic group, necrotic lesions were found containing the inoculated organisms and surrounded by relatively normal brain. In the group treated with antibiotic alone, healed glial scars were found in relatively normal brain. The findings are discussed with reference to the medical literature regarding the influence of glucocorticoids on the inflammatory response and the efficacy of antibiotics when this response is suppressed. 48 references. (Author abstract modified)

000207 Raiteri, Maurizio; Angelini, Francesco; Bertollini, Alberto. Instituto de Farmacologia, Universita Cattolica, Facolta di Medicina, Via della Pineta Sacchetti 644, Rome 00168, Italy **Comparative study of the effects of mianserin, a tetracyclic antidepressant, and of imipramine on uptake and release of neurotransmitters in synaptosomes.** Journal of Pharmacy and Pharmacology (London). 28(6):483-488, 1976.

A comparative study in rats of the effects of mianserin, a tetracyclic antidepressant, and of imipramine on the uptake and release of neurotransmitters in synaptosomes is presented. Both drugs inhibited (3H)noradrenaline (3H-NA) uptake in the hypothalamus, but could not increase 3H-NA release from noradrenergic nerve endings or have an effect on 3H-DA transport mechanisms in striatal synaptosomes. Imipramine was stronger than mianserin in inhibiting 3H5-hydroxytrptamine (3H-5-HT) accumulation by striatal synaptosomes. In contrast mianserin stimulated 3H-5-HT release whereas imipramine was ineffective. Mianserin had virtually no inhibitory activity on 3H-5-HT uptake by rat blood platelets. Imipramine was a modest inhibitor of 3H-gamma-aminobutyric acid (3H-GABA) accumlation by whole brain synaptosomes; mianserin had no effect. Both drugs did not alter 3H-GABA release. These results indicate that minaserin interferes in a way different from that of tricyclic depressants with the neurotransmitter transport mechanisms at the presynaptic level. 21 references. (Author abstract modified)

000208 Rebec, George Vincent. University of Colorado, Boulder, CO **Neurophysiological correlates of long-term amphetamine treatment in rats. (Ph. D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-11605 HC$15.00 MF$8.50 287 p.

Neurophysiological correlates of long-term amphetamine treatment in rats were studied through neuronal activity and reticular formation mechanisms. The response to d-amphetamine in the caudate nucleus and reticular formation of saline pretreated rats was found to parallel that in naive animals, while amphetamine induced alterations in neuronal activity recorded from rats exposed to amphetamine over progressive periods. Duration of amphetamine induced depression of caudate activity tended to increase with prolonged treatment, and could be blocked by subsequent administration of haloperidol. Initial drug induced potentiation of activity was also enhanced following long-term treatment as was duration of the amphetamine induced increase in activity in the reticular formation. Progressive augmentation of neuronal responses to amphetamine and apomorphine following chronic amphetamine treatment supports previous behavioral observations and suggests that a heightened sensitivity of catecholamine receptors may contribute to enhanced effects of long-term amphetamine treatment, compatible with the suggestion of drug induced alterations in catecholamine receptor sensitivity underlying pathophysiology of some human psychotic disorders. (Journal abstract modified)

000209 Redgrave, Peter; Horrell, R. Ian. Department of Psychology, The University, Hull HU6 7RX, England **Potentiation of central reward by localised perfusion of acetylcholine and 5-hydroxytryptamine.** Nature (London). 262(5566):305-307, 1976.

A modified push/pull perfusion system was developed and used to assess the effect of acetylcholine (ACh) and 5-hydroxytryptamine (5-HT) on self-stimulation behavior in the rat. Median forebrain bundle (MFB) self-stimulation via a monopolar stimulating electrode is potentiated by localized perfusions of 5-HT in the ventral mesencephalon (VM). When ACh is perfused in the VM, MFB self-stimulation is increased significantly by low concentrations but decreases to below baseline levels as the concentration of ACh in the perfusate is increased. It is suggested that 5-HT and ACh may excite, directly or indirectly, the dopaminergic cell bodies known to be present in the VM and that a possible anatomical substrate for the proposed interaction between serotonergic systems and catecholaminergic systems involved in central reward has been demonstrated. The modified push/pull system described permits repeated perfusions of a given animal without causing excessive physical trauma to the brain. 14 references.

000210 Rosner, H. Zoologisches Institut der Universitat Stuttgart-Hohenheim, Emil-Wolff-Strasse, D-7000 Stuttgart 70, Germany **/Effect of chlorpromazine on the incorporation of sialic acid into gangliosides and glycoproteins of the chicken brain./** Hemmung des Sialinsaureeinbaus in Ganglioside und Glykoproteine des Kukenhirns durch Chlorpromazin. Psychopharmacology (Berlin). 48(1):25-29, 1976.

The effect of i.p. injected chlorpromazine (CP, 2.5or 5mg/animal) on the incorporation of N-(3H)-acetylmannosamine into glycoprotein bound and ganglioside bound sialic acid, and 14C-histidine into the proteins of the cerebrum, the optic lobes, and the cerebellum after incorporation periods of 1-24 h is studied in the chicken brain. All experiments were performed under constant temperature conditions. Results indicated: 1) the incorporation of 14C-histidine into the proteins of the optic lobes was not influenced by CP; 2) within 24 h in the optic lobes neither the concentration of particle bound sialic acid nor the content of radioactive labeled sialic acid

precursor was affected by the drug; 3) the rate of incorporation of labeled sialic acid into glycoproteins and gangliosides was (up to 6 h after the injection of the precursor) much lower in the CP treated animals than in controls; and 4) the inhibition was the most intensive in the cerebrum (up to 80%), lower in the optic lobes (up to 70%), and only small in the cerebellum (up to 20%), but was always the same for glycoproteins and gangliosides. The different inhibition rates in the different structures may indicate a correlation between the pharmacologic, sedative effects of the drug and the diminished turnover of sialo compounds. 17 references. (Author abstract modified)

000211 Ross, Robert A.; Joh, Tong H.; Reis, Donald J. Laboratory of Neurobiology, Department of Neurology, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 **Reversible changes in the accumulation and activities of tyrosine hydroxylase and dopamine-beta-hydroxylase in neurons of nucleus locus coeruleus during the retrograde reaction.** Brain Research (Amsterdam). 92(1):57-72, 1975.

To examine the biochemical events associated with the retrograde reaction in central noradrenergic neurons, changes in the activities of several enzymes subserving the metabolism of catecholamines, including tyrosine hydroxylase (TH), dopamine-beta-hydroxylase (DBH), DOPA decarboxylase (DDC), and monoamine oxidase (MAO), were measured in the nucleus locus coeruleus of rat brain following transection of the ascending axons from neurons in this nucleus by electrolytic lesions of the posterolateral hypothalamus. Such lesions produced a triphasic response in the activities of TH and DBH. Findings show that a reduction in the accumulation of specific enzymes subserving transmitter biosynthesis characterizes a reversible retrograde action of central noradrenergic neurons. The coincidence of the time course of reduced enzyme accumulation with regenerative sprouting from damaged noradrenergic axons, and the absence of classical signs of chromatolysis in locus coeruleus neurons following comparable lesions, suggest that: 1) during the retrograde reaction there may be a reordering of priorities governing accumulation of specific proteins favoring accumulation of those required for reconstitution of cellular processes by sprouting at the expense of proteins utilized in the synthesis of neurotransmitters; and 2) some intrinsic neurons of the CNS may undergo reversible biochemical changes of a retrograde reaction in the absence of the classical morphological appearance of chromatolysis. 56 references. (Author abstract modified)

000212 Ross, Svante B.; Ogren, Sven-Ove; Renyi, Anna L. Research and Development Laboratories, Astra Lakemedel AB, S-15185 Sodertalje, Sweden **(Z)-dimethylamino-1-(4-bromophenyl)-1-(3-pyridyl)propene(H 102/09), a new selective inhibitor of the neuronal 5-hydroxytryptamine uptake.** Acta Pharmacologica et Toxicologica (Kobenhavn). 39(2):152-166, 1976.

An investigation was conducted to determine the effects in mouse brain slices of (Z)-3-dimethylamino-1-(4-bromophenyl)-1-(3-pyridyl)propene (H-102/09), desipramine and chlorimipramine on: 1) inhibition of radiolabeled noradrenaline (NA) uptake; 2) inhibition of radiolabeled dopamine (DA) uptake; 3) inhibition of radiolabeled 5-hydroxytryptamine (5-HT) uptake; and 4) release of previously accumulated radiolabeled NA, radiolabeled DA and radiolabeled 5-HT. The effects of these compounds on reserpine induced hypothermia and sedation and the 5-hydroxytryptophan (5-HTP) syndrome in mice were also studied. H-102/09 is a more selective inhibitor of 5-HT uptake than chlorimipramine in vivo; in vitro chlorimipramine is more active than H-102/09. Desipramine is a very selective inhibitor of NA uptake in vivo and in vitro. The 5-HTP syndrome is potentiated by H-102/09 and chlorimipramine but not by desipramine. The reserpine hypothermia (but not the sedation) is antagonized and reversed by desipramine and by chlorimipramine, but not by H-102/09. It is suggested that: 1) in striatal tissue slices the inhibition of DA uptake may be due to the releasing effect; 2) the effect of desipramine on 5-HT uptake and the effect of H-102/09 on NA uptake may also involve a release component; and 3) the hypothermic action of reserpine may involve NA but not 5-HT. 29 references. (Author abstract modified)

000213 Ross, Svante B.; Renyi, Anna L. Research and Development Laboratories, Astra Lakemedel AB, S-151 85 Sodertalje, Sweden **Inhibition of the uptake of 3H-dopamine and 14C-5-hydroxytryptamine in mouse striatum slices.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(1):56-66, 1975.

The inhibitory activities of a number of compounds on the simultaneous uptake of 3H-dopamine (3H-DA) and 14C-5-hydroxytryptamine (14C-5HT) in the same slices of the mouse striatum were examined. Experiments with inactive DA and 5-HT demonstrated that the uptake of the two amines occurs at different sites. In vitro (+)-amphetamine was 2.7times more potent than the (-)-isomer whereas in vivo this difference was about 6 times. (+)-Amphetamine was also significantly more active than the (-)-enantiomer on the 3H-DA uptake in striatal slices from the rat. The methylester group in cocaine is essential for the inhibitory activity of cocaine, which had similar potencies on the two uptake mechanisms. Benztropine was much more active on the 3H-DA uptake than on the 14C-5-HT uptake. In vivo the amphetamine derivatives including prolintane and methylphenidate were the most active compounds on the 3H-DA uptake, but the 4-substituted amphetamines were more active on the 14C-5-HT uptake. Among other compounds benztropine was as active as (+)-amphetamine on the 3H-DA uptake. None of the compounds tested seem to be useful as model compounds for the selective inhibition of the DA uptake, since they have other pharmacological effects at lower doses. 14 references. (Author abstract)

000214 Ross, Svante B.; Renyi, Anna L. Research and Development Laboratories, Astra Lakemedel AB, S-15185 Sodertalje, Sweden **On the long-lasting inhibitory effect of N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine (DSP 4) on the active uptake of noradrenaline.** Journal of Pharmacy and Pharmacology (London). 28(5):458-459, 1976.

The inhibitory activities of phenoxybenzamine and N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine hydrochloride (DSP-4) on the noradrenaline uptake of the rat brain are compared. Certain dosages of DSP-4 inhibited the uptake of noradrenaline in the cerebral cortex slices of the mouse by 50%. It has about the same activity as that found for (plus) amphetamine. The corresponding value for phenoxybenzamine indicated that it is about 20 times less active than DSP-4. A single high dose of DSP-4 lasted a long time. Since DSP-4 had no effect on the uptake of (3H) dopamine in slices of striatum or on that of (3H)5-hydroxytryptamine in slices of midbrain of the mouse, the inhibition of noradrenaline uptake seems to be specific for this amine. The effect may be due to alkylation of the noradrenaline uptake receptors or to degeneration of noradrenergic neurons, which is now being investigated. In any case, it is suggested that DSP-4 may become a valuable pharmacological tool since it readily penetrates the blood brain barrier and seems to be specific to the noradrenergic neurons. 6 references.

000215 Sampson, S. R.; Aminoff, M. J.; Jaffe, R. A.; Vidruk, E. H. Departments of Physiology and Neurology, University of California, San Francisco, CA 94143 **Analysis of inhibitory effect of dopamine on carotid body chemoreceptors in cats.** American Journal of Physiology. 230(6):1494-1498, 1976.

The inhibitory effect of dopamine on carotid body chemoreceptors was studied in anesthetized cats to determine whether it was dependent on changes in blood flow in the vicinity of the receptors. The blood supply to the carotid body was isolated, and flow was controlled with a perfusion pump. Single-refiber or few fiber recordings were made from the peripheral end of the cut carotid sinus nerve in seven cats. The rate of discharge of 68 chemoreceptor strands increased when flow through the carotid body was stopped. This response was reduced or abolished by dopamine in animals ventilated with either room air (15 strands) or a gas mixture of 95% O2 and 5% CO2 (53 strands). These results suggest that dopamine exerts its inhibitory effect primarily through a direct action on the chemoreceptors rather than by a vasomotor effect in the carotid body. 19 references. (Author abstract)

000216 Sanger, D. J. Department of Psychology, University of Birmingham B15 2TT, P. O. Box 363, Birmingham, England **Scopolamine and adjunctive drinking in rats.** Psychopharmacology (Berlin). 48(3):307-309, 1976.

The possibility that cholinergic mechanisms may be involved in the control of adjunctive behavior was investigated in rats. Scopolamine produced a dose related attenuation of adjunctive drinking which occurred during intermittent delivery of food to food deprived animals. Physostigmine slightly reduced the levels of drinking but the action of scopolamine was not consistently modified. Tolerance to the effect of the highest dose of scopolamine (1mg/kg) occurred. The results do not confirm the view that cholinergic mechanisms are involved in the control of adjunctive behavior. 13 references.

000217 Scatton, B.; Glowinski, J.; Julou L. Rhone-Poulenc Recherches, Direction des Recherches Pharmaceutiques, 9, quai Jules Guesde, F-94400 Vitry/Seine, France **Dopamine metabolism in the mesolimbic and mesocortical dopaminergic systems after single or repeated administrations of neuroleptics.** Brain Research (Amsterdam). 109(1):184-189, 1976.

The effects of single or repeated does of neuroleptics on dopamine (DA) metabolism in the rat neostriatum were compared. Since some researchers have suggested that the antipsychotic properties of the neuroleptics might be related to their actions on dopaminergic transmission in the mesolimbic or mesocortical systems, it was considered of interest to compare the effects of single or repeated doses of neuroleptics on DA synthesis in these two dopaminergic systems. The brains of male rats were used in the experiments. It is suggested that the antipsychotic action of the neuroleptics may be related principally to their effects on dopaminergic transmission in the mesolimbic and/or mesocortical systems. The intensity of the stimulation of DA synthesis caused by acute neuroleptic treatment persisted and even increased after their chronic administration. 17 references.

000218 Schildkraut, J. J.; Roffman, M.; Orsulak, P. J.; Schatzberg, A. F.; Kling, M. A.; Reigle, Th.G. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Effects of short-and long-term administration of tricyclic antidepressants and lithium on norepinephrine turnover in brain.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(4):193-202, 1976.

The effects of acute administration and chronic administration of tricyclic antidepressants (imipramine and desmethylimipramine) and of lithium on turnover of norepinephrine in the rate brain were studied. Norephinephrine turnover in brain is decreased after acute administration of imipramine or desmethylimipramine but tends to increase during chronic administration of these tricyclic antidepressants. There also may be important differences between the effects of acute and chronic administration of lithium salts on norepinephrine turnover in the central nervous system. Such changes in norepinephrine turnover that develop gradually over the course of long-term drug administration may help to explain the need for chronic administration of tricyclic antidepressants or lithium salts in the treatment of patients with affective disorders. 39 references. (Author abstract modified)

000219 Schmeling, William T.; Hosko, Michael J. Dept. of Pharmacology, Medical College of Wisconsin, Milwaukee, WI 53233 **Hypothermia induced by delta9-tetrahydrocannabinol in rats with electrolytic lesions of preoptic region.** Pharmacology Biochemistry and Behavior. 5(1):79-83, 1976.

Two groups of male Sprague-Dawley rats, one group with subsequently confirmed bilateral preoptic region (POR) lesions and a sham operated group, were administered delta9-tetrahydrocannabinol (delta9-THC) intraperitoneally to determine whether systematically administered delta9-THC would induce hypothermia in rats with acute bilateral electrolytic lesion of POR. The lesioned animals developed hyperthermia within 2 h after surgery when compared to the sham operated controls. Both lesioned and nonlesioned rats exhibited hypothermia within 30 min of delta9-THC administration. The hypothermic response to delta9-THC in the lesioned animals was significantly greater and showed a trend toward longer duration than the hypothermia induced in the sham operated controls. These data demonstrate that delta9-THC is able to induce a hypothermic response in rats whose body temperatures were elevated by POR ablation. Although delta9-THC does not appear to act primarily at POR to induce hypothermia, it is evident that an intact POR plays a role in modifying the duration and magnitude of delta9-THC induced hypothermia. 41 references. (Author abstract modified)

000220 Schneiderman, Barbara; Isaacson, Robert L. Department of Psychology, University of Florida, Gainesville, FL 32611 **Pharmacologic changes in performance of normal and brain-damaged rats.** Behavioral Biology. 17(2):197-211, 1976.

Pharmacological changes brought on by administration of chlorpromazine, alpha-methylparatyrosine, parachlorophenylalanine, and physostigmine on differential reinforcement for low rates of responding (DRL) performance of normal and brain-damaged rats were assessed. Drugs were administered at different times during acquisition of a DRL-20 schedule of reinforcement. Normal and neocortically lesioned subjects were benefited by most of the agents used, but Ss with hippocampal damage were relatively insensitive to the various drugs. subjects with hippocampal damage were only affected by high doses of chlorpromazine, alpha-methylparatyrosine, and the lowest dose of physostigmine. The effects of the various drugs on DRL-20 performance of normal subjects indicate that the number of responses made in a test session can be affected by drugs presumably having predominantly either cholinergic or catecholaminergic modes of action. Responses were decreased by physostigmine, alpha-methylparatyrosine, and by low doses of chlorpromazine. Brain-damage changed the subject's reactions to the drugs. A view of the catecholaminergic activation system inhibited by cholinergic

and serotonergic systems was supported by many of the findings. 26 references. (Author abstract modified)

000221 Schulte am Esch, J. Institut fur Anaesthesiologie, 53 Bonn-Venusberg, Neurochirurgische Klinik, West Germany **/Effects of halothane on catecholamine metabolism in the brain stem of rats./** Wirkungen von Halothan auf den Katecholaminstoffwechsel im Hirnstamm von Ratten. Arzneimittel-Forschung (Aulendorf). 26(3):324-327, 1976.

The effects of halothane on catecholamine metabolism in the brain was experimentally studied. In addition to its effects on vegetative efferents, the investigation explored halothane on dopamine and norepinephrine concentrations and on the transformation of L-dopa into dopamine and L-norepinephrine in the brain stems of 118 rats. Anesthesia with 2% vol of halothane reduced dopamine content by 41.4%, and reduced norepinephrine content by 17.8%. These effects could be observed up to 3 h after narcosis. Electrophysiological studies during anesthesia with 2% vol halothane indicate a clear reduction in the sympathetic activity of the CNS both at rest and after central excitation, which returns to normal 70 minutes after narcosis. Administration of L-dopa led to an increase in dopamine by 43.5% within 45 min. This transformation of L-dopa into dopamine is not affected by concurrent halothane anesthesia. There is no increase in norepinephrine after the administration of L-dopa. Thus, the effect of halothane on catecholamine metabolism in the brain stem is due to its influence on the precursors of L-dopa. Halothane inhibits the transport of the L-dopa precursor L-tyrosine from plasma to brain tissue. This inhibition brings about a depression of sympathetic activity. For this reason, dopamine is more important than norepinephrine because of its position in catecholamine metabolism. 29 references. (Journal abstract modified)

000222 Schulz, Rudiger; Herz, Albert. Department of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munchen 40, Germany **Aspects of opiate dependence in the myenteric plexus of the guinea-pig.** Life Sciences (Oxford). 19(8):1117-1127, 1976.

A controlled study investigating specific aspects of the mechanism controlling the tolerant/dependent state of myenteric plexus of guinea pigs is summarized. Longitudinal muscle strips from the ileum, with adherent myenteric plexus, continuously exposed to normorphine, displayed a contracture upon naloxone challenge. This phenomenon represents a sign of abstinence. Remove of the opiate by extensive washing resulted in the failure of naloxone to induce the abstinence sign, while the plexus still displayed considerable, though reduced, tolerance to morphine. Reexposure of withdrawn preparations to normorphine reinduced the ability to display the abstinence sign. Highly tolerant preparations exhibited a 30 fold increase in sensitivity to serotonin and prostaglandin E1 when tested a few minutes after naloxone precipitated withdrawal. Supersensitivity rapidly declined when normorphine was washed off the preparation, while reincubation of withdrawn tissues with the opiate resulted in reinduction of supersensitivity. The data confirm a close relationship between a state of tolerance and dependence (including display of the abstinence sign) and supersensitivity to putative neurotransmitters or neuromodulators, becoming evident following administration of naloxone. 27 references. (Journal abstract)

000223 Schumpelick, V.; Farthmann, E. Universitat Humburg, Universitatskrankenhaus Eppendorf, Chirurgische Klinik, Martinistr. 52, 2 Hamburg, West Germany **/Study of the protective effect of vitamin A on stress ulcer in the rat./** Untersuchung zur protektiven Wirkung von Vitamin A beim Stressulkus der Ratte. Arzneimittel-Forschung (Aulendorf). 26(3):386-388, 1976.

The protective effect of vitamin A on "restraint stress" ulcer formation was studied in rats. Thirty male albino rats, weighing approximately 240g, were given 1,000IU or 2,000IU vitamin A, or 0.2ml 0.9% salt solution i.m. every 6 hours after 19 hours of immobilization. The rats receiving vitamin A showed significantly fewer and smaller ulcers than the controls. There was no difference in effect of the 2 doses of vitamin A. Only a few rats had no gastric ulcers at all, which means the protection was not absolute. Therapeutic use of vitamin A in the prophylaxis of stress ulcer is discussed. 18 references. (Author abstract modified)

000224 Sherman, Arnold D.; Gebhart, Gerald F. Division of Neurochemistry, Department of Psychiatry, University of Iowa, Iowa City, IA 52242 **Morphine and pain: effects on aspartate, GABA and glutamate in four discrete areas of mouse brain.** Brain Research (Amsterdam). 110(2):273-281, 1976.

The effects of restraint stress, pain, morphine, morphine plus pain, pentobarbital plus pain, chlorpromazine plus pain, naloxone plus pain, and morphine plus naloxone plus pain on the levels of aspartate, GABA, and glutamate in the periaqueductal central gray matter, hypothalamus, midbrain reticular formation, and cortex of mouse brain was studied. Of the three neurohumors, only glutamate is systematically altered relative to the experimental manipulations. Of the four brain areas examined, only the periaqueductal central gray matter appears to be a locus of the antinociceptive action of morphine. Morphine also appears to produce a drug specific effect in the hypothalamus which is not related to its analgesic effect. There are no significant pain, restraint stress or drug related effects on the levels of glutamate in either the midbrain reticular formation or the cortex. 17 references. (Author abstract modified)

000225 Short, Peter H.; Shuster, Louis. Department of Biochemistry and Pharmacology, Tufts University School of Medicine, 136 Harrison Ave., Boston, MA 02111 **Changes in brain norepinephrine associated with sensitization to d-amphetamine.** Psychopharmacology (Berlin). 48(1):59-63, 1976.

The development of d-amphetamine sensitization in mice was investigated, and the relationship of brain catecholamines to this sensitization was examined. Pretreatment of B6AF/J mice with d-amphetamine HCl 10mg/kg, twice daily for 5 days, produced a four fold increase in the running response to test dose of 5mg/kg amphetamine. Amphetamine pretreatment decreased whole brain norepinephrine levels to 50% of control values and whole brain dopamine to 85%. The test dose of 5mg/kg amphetamine lowered whole brain norepinphrine levels of control mice. In amphetamine pretreated mice, this injection caused an increase in whole brain norepinphrine levels at 30 min, followed by a decrease at 60 min. No change in whole brain dopamine levels was observed in either group. Amphetamine sensitization and norepinephrine depletion were still evident 25 days after pretreatment. No cross sensitization to morphine or cocaine was observed. Reserpine pretreatment resulted in a three fold increase in locomotor activity following injection of d-amphetamine, 5mg/kg. No sensitization or changes in catecholamine levels were observed in amphetamine treated A/J mice. These results suggest that the sensitization produced by amphetamine pretreatment by be related to the depletion of brain norpinephrine. 41 references. (Author abstract modified)

000226 Shulgin, Alexander T.; Dyer, Donald C. 1483 Shulgin Road, Lafayette, CA 94549 **Psychotomimetic phenylisopropylamines. 5. 4-alkyl-2,5-dimethoxyphenylisopropylamines.** Journal of Medicinal Chemistry. 18(12):1201-1204, 1975.

A homologous series of 4-alkyl-2,5-dimethoxyphenylisopropylamines was synthesized and compared with mescaline as serotonin agonists in a sheep umbilical preparation. The three carbon homolog 6d was found to be the most potent of the straight chain series in accordance with its observed psychotomimetic effectiveness in man. 17 references. (Author abstract modified).

000227 Siegel, Shepard. Department of Psychology, McMaster University, Hamilton, Ontario L8S 4K1, Canada **Morphine analgesic tolerance; its situation specificity supports a Pavlovian conditioning model.** Science. 193(4250):323-325, 1976.

Rats were made tolerant to morphine in either of two environments and then assessed for morphine induced alteration of pain sensitivity in both environments. Analgesic tolerance was displayed when rats were tested in that environment in which they previously received morphine, but not in the alternative environment. The results indicate that an association between environmental cues and the systemic effects of morphine is crucial to tolerance development. The findings, although contrary to most theories of tolerance, are predicted by the conditioning theory of tolerance, which stresses the role of drug associated environmental cues in the display of tolerance. 9 references. (Author abstract modified)

000228 Singh, P. P.; Das, P. K. Department of Pharmacology, Institute of Medical Sciences, Banaras Hindw University, Varanasi-221005, India **Role of catecholamines in the hypothermic activity of cannabis in albino rats.** Psychopharmacology (Berlin). 50(2):199-204, 1976.

The role of brain monoamines in mediating the hypothermic response to orally administered cannabis resin (CI) was studied in rats using agents which influence monoamine synthesis, storage, release, reuptake, metabolism and receptor activity and monoaminergic neuronal activity. The hypothermic activity of CI was potentiated by nialamide and parachlorophenylalanine, unaffected by 5, 6-dihydroxytryptamine and alpha-methyldopa, blocked by alpha-methyl-metatyrosine, alpha-methyl-paratyrosine, 6-hydroxydopamine, gammabutyrolactone, phentolamine, propranolol and chlorpromazine and inhibited by diethyldithiocarbamate, diethyldithiocarbamate plus L-DOPA, and phenoxybenzamine. CI induced hyperthermia in tolerant rats could be reversed to hypothermia by imipramine. Reserpine induced hypothermia was blocked by nialamide, alpha-methyl-paratyrosine, 6-hydroxydopamine and chlorpromazine. There was a partial cross-tolerance between cannabis and reserpine. It is suggested that the hypothermic activity of CI is mediated through noradrenaline, and not by dopamine or serotonin. The mechanism of action of cannabis and reserpine on noradrenergic neurones seems to be different. 29 references. (Author abstract modified)

000229 Smith, Robert V.; Erhardt, Paul W.; Neumeyer, John L.; Borgman, Robert J. Drug Dynamics Institute, College of Pharmacy, University of Texas at Austin, Austin, TX 78712 **Metabolism in vitro of potential apomorphine prodrugs.** Biochemical Pharmacology (Oxford). 25(18):2106-2107, 1976.

The hypothesis that the activity of several analogs of apomorphine is related to their metabolic conversions to apomorphine or N-n-propylnorapomorphine was investigated using a rat liver microsomal preparation. Apocodeine and isoapocodeine are both converted to apomorphine in vitro; however, apocodeine is metabolized to a greater extent than is isoapocodeine. No evidence was found for the microsomal hydroxylation of 10-hydroxyapomorphine to apomorphine or for 10-hydroxy-N-n-propylnorapomorphine to N-n-propylnorapomorphine. It is suggested that 10-hydroxy-N-n-propylnorapomorphine may have a direct dopaminergic agonist action. 18 references.

000230 Smits, Jos F.; Struyker-Boudier, Harry A. Department of Pharmacology, University of Nijmegen Medical School, Nijmegen, The Netherlands **Intrahypothalamic serotonin and cardiovascular control in rats.** Brain Research (Amsterdam). 111(2):422-427, 1976.

The cardiovascular effects of serotonin after injection into circumscribed areas of the brain were studied in rats. Injection of serotonin into the anterior hypothalamic/preoptic region (AH/PO), but not into other areas of the hypothalamus, causes a substantial, immediate rise in blood pressure. In some animals, a slight decrease in heartrate also occurs. The minimal doses of serotonin which produce a significant increase in blood pressure are 3ng to 10ng after intrahypothalamic injection and 50ng to 100ng after intraventricular injection. Intraventricular pretreatment with the antiserotonin agent methysergide substantially reduces the blood pressure response to serotonin but intrahypothalamic pretreatment with methysergide produces a reduction in the blood pressure response to serotonin which is not statistically significant. It is suggested that the blood pressure response to intrahypothalamic serotonin and to intraventricular serotonin is produced by stimulation of serotonin receptors in the AH/PO region. The possibility that serotonin may also produce cardivascular effects at different levels of the CNS should be considered. It is also suggested that the antagonism caused by intraventricular methysergide may be due to an extrahypothalamic effect. 18 references.

000231 Speiser, Zipora; Weinstock, Marta. Department of Physiology and Pharmacology, Sackler School of Medicine, Tel Aviv University Ramat Aviv, Israel **Reduction by propranolol of raised urinary output of MHPG in hyerpactive rats.** Pharmacology Biochemistry and Behavior. 4(5):531-534, 1976.

Experiments were conducted to determine: 1) whether isolation induced hyperactivity in rats results from an increased turnover of central noradrenaline (NA) or peripheral NA, reflected by elevated urinary 3-methoxy-4-hydroxyphenylglycol (MHGP) excretion; 2) whether the selective tranquilizing effect of propranolol is associated with a reduction in MHPG output; and 3) the usefulness of the isolated rat as a model for hyperactivity states involving increased NA release. Prolonged isolation of rats results in hyperactivity in the open-field and significantly increases 24 hr urinary excretion of MHPG when compared with control animals. Exposure of group housed rats to 4 degrees C for 2 hr also increases urinary excretion of MHPG. Pretreatment of isolated rats with Dl-propranolol, d-propranolol or proctolol: 1) abolishes hyperactivity of isolated rats; 2) reduces MHPG output in isolated rats; and 3) reduces MHPG output in rats exposed to cold. Open-field activity of group housed rats are not reduced by dl-propranolol. It is suggested that propranolol may have a selective inhibitory effect on emotional stress induced and physical stress induced increases in NA turnover. 19 references. (Author abstract modified)

000232 Stange, G; Benning, C. D.; Degenhardt, M.; Ottinger, E. UniversitatscHNG-Klinik, Killianstr. 5, 78 Freiburg/Brsg., West Germany /**Adaptational behavior of peripheral and central responses in guinea pigs under the influence of various fractions of an extract from Gingko biloba.**/ Adaptationsverhalten peripherer und zentraler akustischer Reizantworten des Meerschweinchens unter dem Einfluss verschiedener Fraktionen eines Extraktes aus Ginkgo biloba. Arzneimittel-Forschung (Aulendorf). 26(3):367-374, 1976.

Experimental studies on 114 guinea-pigs proved definitely the influence of an extract from Ginkgo biloba batch no. 02 on the acoustic system. Experiments with animals ensured that the adaptation of excitation of the organ of Corti is significantly influenced. This result is shown by registrations of the acoustic nerve potentials in the adapted and nonadapted state. The relation of excitation to adaptation is significantly changed. Under adaptation of excitation an influence on the metabolism of involution is probable. The slow evoked potentials of the acoustic cortex showed no additional influence on the central auditory pathways. With the Ginkgo biloba extract it is probably possible to diminish sound damage caused by white noise. Further experiments on animals are necessary to ensure the application of this pharmaceutical preparation for clinical use. 80 references. (Author abstract)

000233 Stefanini, Ennio; Fadda, Fabio; Medda, Lucio; Gessa, Gian Luigi. Institute of Pharmacology, University of Cagliari, I-09100 Cagliari, Italy **Selective inhibition of serotonin uptake by trazodone, a new antidepressant agent.** Life Sciences (Oxford). 18(12):1459-1466, 1976.

The inhibitory effect of trazodone, a nontricyclic antidepressant, on 5-HT and catecholamine uptake into the synaptosomal preparation from the rat brain was compared with that of chlorimipramine. The inhibition of 5-HT uptake by trazodone is competitive with a Ki of 1.6x 10 to the minus 6M. Trazodone inhibits 3H-5-HT, 3H-NE, and 3H-DA uptake with an IC50 of 1.4x 10 to the minus 6, 3.1x 10 to the minus 4, and 5.2x 10 to the minus 4M, respectively. Therefore trazodone is 220 and 370 times more potent in inhibiting 5-HT than NE and DA uptake, respectively. The respective IC50 values of chlorimipramine were 0.9x 10 to the minus 7, 3.6x 10 to the minus 6, and 4.0x 10 to the minus 6M for 3H-5HT, 3H-NE, and 3H-DA. 36 references. (Author abstract)

000234 Stinus, L.; Thierry, A. M.; Cardo, B. Laboratoire Psychophysiologie, University de Bordeaux I, Ave des Facultes, F-33 405 Talence, France **Pharmacological and biochemical studies of intracranial self-stimulation: roles of dopaminergic and noradrenergic neuronal systems with electrodes either in area ventralis tegmenti on in lateral hypothalamus.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 280-283).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium in April 1975, the results of studies into the importance of dopamine (DA) and noradrenaline (NA) neuronal systems in catecholaminergic control of intracranial self-stimulation (ICSS) in the area ventralis tegmenti (AVT) and in the dorsal part of the lateral hypothalamus (LH) are reported. In both AVT and LH implanted rats pretreated with reserpine, nearly total blockade of both DA and NA synthesis by alpha-methyl-paratyrosine (AMPT), reduced ICSS responses; blockade of NA synthesis alone by FLA-63 did not. Apomorphine, a DA receptor agonist, reinstated the inhibited ICSS in both AVT and LH rats. Levo-dihydroxyphenylalanine, a precursor of both DA and NA, also reinstated both AVT and LH ICSS after AMPT inhibition; racemic threo-dihydroxyphenylserine, a precursor of NA alone, reinstated ICSS only in AVT rats. It is concluded that AVT ICSS is probably under the control of both DA and NA mechanisms, while only a DA link seems to be involved in ICSS obtained by electrodes implanted in the LH location. 4 references.

000235 Stoff, David M.; Wyatt, Richard J.; Gillin, J. Christian. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, William A. White Building, Washington, DC 20032 **Parachlorophenylalanine potentiates facilitatory effects of mescaline Shuttlebox escape/avoidance in rats.** Psychopharmacology (Berlin). 47(3):287-292, 1976.

The effects of serotonin synthesis inhibition by parachlorophenylalanine (pCPA) on mescaline induces facilitation of shuttlebox avoidance were studied in rats. Acute pCPA pretreatment potentiates facilitatory effects of mescaline on shuttlebox escape/avoidance in hooded rats both during acquisition of avoidance behavior and in stable pretrained poor avoiders. pCPA alone does not influence avoidance behavior in either situation. Mescaline, with pCPA pretreatment, may be associated with long-term interference with avoidance performance; all rats treated with this combination are later found to be poor avoiders, unable to achieve a stable baseline of good avoidance. pCPA significantly depletes brain norepinephrine and dopamine as well as serotonin. It is suggested that depletion of brain serotonin by pCPA may: 1) lead to a functional change in the catecholaminergic system; 2) reduce serotonin's inhibitory influence; 3) stimulate the catecholaminergic system; and 4) allow mescaline to exert a stronger effect on behavior. 35 references. (Author abstract modified)

000236 Stoof, J. C.; Schipper, J.; Mulder, A. H. Department of Neurology, Free University, Medical Faculty, Van der Boechorststaat 7, Amsterdam, The Netherlands **On the specificity and mechanism of action of m-tyrosine in antagonizing the central effects of reserpine in rats.** Neuropharmacology (Oxford). 15(7):379-382, 1976.

The effects of both m-tyrosine and L-DOPA on reserpine induced depletion of brain dopamine were studied. The influence of pretreatment with reserpine, DOPA and m-tyrosine on the in vitro uptake and release of radio labelled dopamine in brain tissue was also investigated. m-Tyrosine, when given in repeated doses shortly before and after injection of reserpine, partially but significantly antagonizes the dopamine depleting action of reserpine in the brain. Pretreatment with m-tyrosine also partially protects against the marked reductions in synaptosomal 3H-dopamine uptake and in release of 3H-dopamine from striatal tissue slices prepared from rats pretreated with reserpine. 5-Hydroxytryptophan and DOPA also appear to have a protective action against reserpine, comparable with that of m-tyrosine. It is suggested that the interaction between m-tyrosine and reserpine, resulting in protection of the dopamine stores against depletion, is not a specific effect. 17 references. (Author abstract modified)

000237 Strange, A. W.; Schneider, C. W.; Goldbort, R. Psychology Department, Patuxent Institution, Jessup, MD **Selection of C3 alcohols by high and low ethanol selecting mouse strains and the effects on open field activity.** Pharmacology Biochemistry and Metabolism. 4(5):527-530, 1976.

An experiment was conducted to determine whether the tolerance and selection relationships previously observed in various strains of mice after administration of 1,2-propanediol

exist for other C3 alcohols as well. Mice of the high ethanol selecting C57BL/6j strain consume significantly larger amounts of 10% solution of 1,3-propanediol and 10% solution of 1-propanol than the low ethanol selecting DBA/2j strain. Both strains uniformly avoid a 10% solution of 1,3-propanediol and 10% of 2-propanol. Open-field activity was tested 30 min after an IP injection of three different equimolar doses of each alcohol. An increase in activity was produced in the DBA/2j strain by high doses (0.003ml/mg) and middle doses (0.0015ml/mg) of 1,2-propanediol and by a low dose (0.0005 ml/mg) of 2-propanol. The C57BL/6j strain were unaffected by these doses. High doses of 2-propanol produced sleep in both strains with the DBA/2j strain sleeping significantly longer, and 1,3-propanediol produced depression in both strains. Death resulted in all animals following injections of the high dose (0.002ml/gl) and medium doses (0.001ml/gm) of 1-propanol while the low dose (0.0005ml/gm) produced slight depression. It is suggested that high alcohol drinking strains of mice and low alcohol drinking strains of mice possess a differential neural sensitivity to some alcohols. 16 references. (Author abstract modified)

000238 Strocchi, P.; Gandolfi, O.; Montanaro, N. Institute of Pharmacology, University of Bologna, Bologna, Italy **Effect of single and repeated administration of sulpiride on the restraint ulcer in the rat.** Arzneimittel-Forschung (Aulendorf). 26(3):419-421, 1976.

The preventive action of N-ethyl-2 (2-methoxy-5-sulfamidebenzamidomethyl)-pyrrolidine (sulpiride, Dobren) on restraint ulcer was studied in 80 albino male Wistar and Sprague-Dawley rats in a 5x2x2 factorial design, with single or repeated injections of saline, 5, 10, 20, or 40mg/kg i.p. The Wistar strain was shown to be less sensitive to the ulcerogenic procedure and a significant preventive effect of sulpiride occurred only at the dose of 10mg/kg. In the Sprague-Dawley strain a preventive effect was present not only at this dose, but also at 20mg/kg and 5mg/kg, the latter giving the greatest effect. Animals receiving 50mg/kg i.p. did not differ significantly from control in both strains. Results are discussed in relation to possible changes of the cerebral monoamine turnover during the establishment of stress ulcer, particularly in terms of restoration of the balance between dopamine and norepinephrine neuronal activity. 21 references. (Author abstract modified)

000239 Szekely, J. I.; Dunai-Kovacs, Zsuzsa; Borsy, J. Research Institute for Pharmaceutical Industry, Szabadsagharcosok utja 47/49, H-1045 Budapest, Hungary **The effect of antiparkinsonian drugs on chlorpromazine-induced depression of operant behaviour.** Pharmacology (Basel). 14(3):240-246, 1976.

The hypothesis of Davies et al (1973) that reversal of neuroleptic induced conditioned reflex inhibition is a specific property of dopaminergic antiparkinsonian drugs was reexamined. Rats were conditioned in automatic Skinner boxes on a discrete trial avoidance/escape schedule. The chlorpromazine induced conditioned reflex inhibition is reversed by the dopaminergic stimulants apomorphine and amantadine, but not by the central anticholinergic agents atropine, trihexyphenidyl and diethazine. It is suggested that the reversal of neuroleptic induced conditioned reflex inhibition may be a useful tool in differentiation of the two classes of antiparkinsonian agents. It is concluded that additional evidence for the crucial role of dopaminergic mechanisms in the maintenance of conditioned behavior has been presented. 28 references. (Author abstract modified)

000240 Thierry, A. M.; Tassin, J. P.; Blanc, G.; Glowinski, J. College de France, Groupe NB, F-75231 Paris Cedex 05, France **Topographic and pharmacological study of the mesocortical dopaminergic system.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 290-293).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium in April 1975, research using new biochemical techniques to analyze precisely the topographical distribution of dopaminergic nerve terminals in the anterior part of the rat cerebral cortex and to localize the dopaminergic cell bodies sending axons to the frontal cortical area is reviewed. The effects of some psychotropic drugs on cortical dopamine (DA) metabolism were studied. Thioproperazine increased, while apomorphine decreased, DA synthesis in cortical tissue slices from both normal and 6-hydroxydopamine lesioned rats. It is concluded that the mesocortical dopaminergic neurons are sensitive to the effects of neuroleptics and apomorphine and that these findings should be considered in elucidating the mechanisms involved in the antipsychotic actions of neuroleptics. 15 references.

000241 Toda, N. Department of Pharmacology, Faculty of Medicine, Kyoto University, Kyoto 606, Japan **Influence of dopamine and noradrenaline on isolated cerebral arteries of the dog.** British Journal of Pharmacology (London). 58(1):121-126, 1976.

Effects of dopamine and noradrenaline were compared in helically cut strips of canine cerebral arteries. Dopamine caused a greater maximal contraction than noradrenaline, although the ED50 for noradrenaline was appreciably less. The contraction induced by these amines was reversed to a relaxation by treatment with phenoxybenzamine. Relaxation induced by dopamine phenoxybenzamine treated and prostaglandin contracted cerebral arteries was not influenced by 1 microM propranolol, while relaxation induced by noradrenaline at low concentrations (2 microM and 10 microM) was significantly attenuated. Neither aminophylline nor atropine affected the relaxant effect of dopamine. It is concluded that a mechanism other than beta-adrenergic, cholinergic or adenosine related appears to be involved in the relaxation elicited by dopamine in cerebral arterial strips. 15 references. (Author abstract modified)

000242 Trabucchi, M.; Spano, P. F.; Tonon, G. C.; Frattola, L. Department of Pharmacology, University of Brescia, Italy **Effects of bromocriptine on central dopaminergic receptors.** Life Sciences (Oxford). 19(2):225-231, 1976.

Pharmacokinetic effects of bromocriptine injected in rats on central dopaminergic receptors were studied. Bromocriptine injected to rats induces an increase of cAMP levels in the striatum in vivo. The time course of this increase is very similar to that of apomorphine. However, bromocriptine does not stimulate striatal dopamine sensitive adenylate cyclase, but instead antagonized the activation of this enzyme elicited by dopamine. Possible hypotheses on various sites of action of the drug are discussed. The stimulating effect of the drug is ascribed to a dopaminergic mechanism, using the turnover rate of cAMP as a reliable biochemical correlate of the behavioral effect. A blocking activity of the drug on the dopaminergic system was also noted in some recent experiments in Parkinsonian patients, indicating the need for further research on modes of action of bromocriptine. 23 references. (Journal abstract modified)

000243 Trafton, Clinton L.; Kowalczyk, Lucretia; MacLeod, Richard. Department of Psychology, University of Arizona, Tuscon, AZ 85721 **The effects of bilateral cingulate cortex leisons on morphine withdrawal symptoms in rats.** Physiological Psychology. 4(2):149-150, 1976.

In order to test the hypothesis that bilateral cingulate cortex lesions prevent opiate dependence and associated withdrawal symptoms, rats were given access to sucrose morphine solutions and subsequently challenged with nalorphine, an opiate antagonist. Animals with cingulate cortex lesions lost more weight following the nalorphine challenge than other animals, indicating that the lesions do not prevent withdrawal symptoms. On the contrary, the lesions are associated with more severe symptoms and, by inference, physiological dependence as well. 3 references. (Author abstract)

000244 Tsujimoto, A.; Dohi, T. Department of Pharmacology, Hiroshima University School of Dentistry Kasumi, Hiroshima, Japan **Characteristics of sustained tremor induced by nicotine in pilocarpine-treated animals.** Neuropharmacology (Oxford). 15(7):421-426, 1976.

Sustained tremor was produced by administration of nicotine to pilocarpine pretreated mice and rats and the characteristics of the tremor were studied; in addition, the effectiveness of a variety of drugs in blocking the induction of tremor were investigated. The tremor produced by nicotine and pilocarpine is composed of tremor of the head and limbs and occasional sharp head movements up and backwards. Pilocarpine causes hyperthermia in most of the rats kept in a high ambient temperature (approximately 22 degrees C). Nicotine produces the sustained tremor only in rats showing a rise in body temperature due to pilocarpine pretreatment. In mice pretreated with pilocarpine, nicotine produces the sustained tremor under normal conditions as well. The time course of nicotine elimination from the brain is dissociated from that of the intensity and duration of the sustained tremor. Atropine, nicotinolytic drugs, promethazine, phenobarbital and propranolol block the induction of the tremor. L-Dihydroxyphenylalanine, alpha-methyldopa, reserpine and tolazoline are not effective. It is suggested that tremor produced by nicotine and pilocarpine does not result solely from the inhibition of hepatic drug metabolism by pilocarpine, and that the central cholinergic system may be involved in the induction of this tremor. This method of inducing tremor may not be useful in the search for anti-Parkinson drugs but may be useful in studying mechanisms involved in tremor. 26 references. (Author abstract modified)

000245 Turnbull, M. J.; Watkins, J. W. I.C.I. Ltd, Alderley Park, Alderly Edge, Cheshire, England **Determination of halothane-induced sleeping time in the rat: effect of prior administration of centrally active drugs.** British Journal of Pharmacology (London). 58(1):27-35, 1976.

A method is described for the determination of halothane induced sleeping time in the rat. The sleeping time exhibited a diurnal variation which was due, at least in part, to a change in the sensitivity of the central nervous system (CNS) to the anaesthetic. A tolerance to halothane was induced by pretreatment of rats with doses of amylobarbitone, pentobarbitone or meprobamate sufficient to keep animals anaesthetized for approximately 12 hr. This tolerance was followed by a period of halothane hypersentitivity. Halothane tolerant animals awakened with higher brain halothane concentrations and were also tolerant to intracerebroventricularly administered pentobarbitone. Halothane hypersensitive rats awakened with lower brain halothane concentrations and were also hypersensitive to intracerebroventricularly administered pentobarbitone. The possibility that the induction of cross tolerance to halothane may be indicative of the potential of drug to produce dependence is discussed. 14 references. (Author abstract modified)

000246 Usdin, Earl. Psychopharmacology Research Branch, National Institute of Mental Health, Rockville, MD **Workshop on para-chloroamphetamine.** Psychopharmacology Bulletin. 12(3):51-74, 1976.

Abbreviated versions of eight papers presented at a workshop on para-chloroamphetamine (PCA) are presented. Topics of the papers were: 1) PCA effects on turnover of brain catecholamines; 2) the effects of intraventricularly administered PCA and its analogs; 3) metabolism of PCA in rats; 4) pharmacology of PCA and analogs; 5) long-term effects of PCA on central serotonergic mechanisms; 6) the effect of PCA on behavior; 7) neurotoxic action of PCA in the rat; and 8) 4-chloroamphetamines: chance and trend in the development of new antidepressants. The conclusions from the workshop are: 1) PCA has antidepressant activity; 2) PCA may have many of the properties of amphetamine without having its addictive potential; and 3) PCA produces B-9 neuronal destruction and this neurotoxic effect seems to rule out further clinical testing of PCA in humans. The eight papers have a total of 89 references.

000247 Valenti, Piero; Fanelli, Ottorino; Da Re, Paolo; Cima, Lorenzo. Department of Chemistry, University of Pisa, Pisa, Italy **Structure-activity relationships in centrally stimulating xanthone derivatives. Part XII. Some open models and conclusive remarks.** European Journal of Medicinal Chemistry (Paris). 10(4):394-397, 1975.

Aspects of the structure/activity relationships among the central nervous system (CNS) stimulating xanthone derivatives 1a-e (N-disubstituted 3-methoxy-4-aminomethylxanthones) are examined in mice from 3 different articles. Some open models related to compound 1 such as the benzophenone derivatives 7 and 8a-e, originating by the opening of the gamma-pyrone ring of 1 as well as more simple derivatives such as 9a-e which reproduce only the substituted benzene ring of 1 are discussed. Pharmacological results for the 3 articles are presented. The modifications described in the articles appear to cause a lowering of the CNS stimulating activity as well as a change of the stimulating pattern. Some conclusive remarks are presented and the critical sizes of a possible receptor site involved in the CNS stimulating activity of this type of compound is tentatively suggested. 20 references.

000248 van Zwieten, P. A. Division of Pharmacotherapy, Department of Pharmacy, Plantage Muidergracht 24, Amsterdam-C, The Netherlands **The reversal of clonidine-induced hypotension by protriptyline and desipramine.** Pharmacology (Basel). 14(3):227-231, 1976.

The interaction between clonidine and tricyclic antidepressants was studied. The pronounced central hypotensive action of 1 microgram clonidine/kg, administered into the left vertebral artery of chloralose anesthetized cats readily reversed by protriptyline (300 microgram/kg) or desipramine (300 microgram/kg), infused via the same route shortly after the development of the maximum hypotensive effect of clonidine. Pretreatment with tricyclic antidepressants significantly diminishes the central hypotensive action of clonidine. This interaction has been presumed to occur at the level of central alpha-adrenoreceptors, where clonidine would be the agonist and tricyclic antidepressants the antagonist. It is suggested that

a competitive antagonism at the central level may be involved. 13 references. (Author abstract modified)

000249 Verhoef, J.; Witter, A. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, Utrecht, The Netherlands **In vivo fate of a behaviorally active ACTH 4-9 analog in rats after systemic administration.** Pharmacology Biochemistry and Behavior. 4(5):583-590, 1976.

The in vivo fate of a three fold substituted radiolabelled ACTH 4-9 analog with a markedly potentiated behavioral activity (4-Met(02),8-D-Lys,9-Phe-ACTH 4-9) was investigated in rats. Plasma concentrations of total radioactivity and intact peptide were determined at various periods after IV, SC, or oral administration of approximately 40 microgram doses to urethane anesthetized animals. The drug was also administered orally to conscious animals. Maximal plasma concentrations are reached 8 min after SC injection. Maximal plasma levels are reached 8 hr after oral administration to anesthetized rats and 4 hr after oral administration to conscious rats. The initial volume of distribution is 5.9% of body weight and the initial half-life (t1/2) for intact peptide is 4 min. Shortly after IV administration and SC administration, relatively high plasma levels and relatively stable plasma levels of intact peptide are obtained, indicating metabolic stability. Determination of metabolite patterns in trichloracetic acid extracts of plasma and brain by paperchromatography and paperelectrophoresis also indicates metabolic stability. The plasma profiles indicate increased stability of the labile 8Lys-9Phe bond by the introduction of an 8-D-Lys. Formation of tritiated water occurs in brain and in the gastrointestinal tract; proteolysis i n these compartments is higher than in plasma. High uptake of radioactivity occurs in the kidney, but urinary excretion is low during the first 30 min. Uptake in brain is low and parallels uptake in cerebrospinal fluid. It is suggested that the increased behavioral activity of the ACTH 4-9 analog can be explaine d by stabilization against proteolytic breakdown. 19 references. (Author abstract modified)

000250 Vetulani, Jerzy; Stawarz, Robert J.; Dingell, James V.; Sulser, Fridolin. Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland **A possible common mechanism of action of antidepressant treatments.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 293(2):109-114, 1976.

A possible common mechanism of action of antidepressant treatments was sought in research with male Sprague-Dawley rats. The response of the norepinephrine (NE) sensitive cyclic AMP generating system in slices of rat limbic forebrain after both acute and chronic administration of tricyclic antidepressants, desipramine (DMI) and iprindole, as well as electroconvulsive treatment (ECT) was investigated. Neither the basal level of cyclic AMP nor the hormonal response to NE were altered after administration of a single dose or short-term treatment with DMI and iprindole. However, administration of antidepressants on a clinically more relevant time basis markedly reduced the sensitivity of the cyclic AMP generating system to NE. This change in sensitivity was not related to the levels of drugs in the brain. The response of cyclic AMP to NE was also reduced by ECT, but onset of this action was shorter than that observed with antidepressants. ECT also antagonized the enhanced response of cyclic AMP to NE following destruction of central adrenergic nerve terminals with 6-hydroxydopamine. It thus appears that the therapeutic action of tricyclic antidepressants could be related to postsynaptic adaptive changes in the sensitivity of noradrenergic adenylate cyclase receptor system rather than to acute presynaptic events. 34 references. (Author abstract modified)

000251 Waldeck, Bertil. Dept. of Pharmacology, Univ. of Goteborg, Fack, S-400 33 Goteborg, Sweden **On the interaction between caffeine and barbiturates with respect to locomotor activity and brain catecholamines.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(2):172-180, 1976

Mice were first given 10mg/kg caffeine or saline, and 30 min later pentobarbitone, 4-32mg/kg. Both drugs caused an increased locomotor activity per se. However when 16mg/kg pentobarbitone was given after caffeine, the effects appeared to be more than additive. Similar results were obtained when phenobarbitone was substituted for pentobaritone, and also when the order caffeine/phenobarbitone was reversed. In another experiment mice received reserpine, 10mg/kg, 6 hrs before the combined treatment with ET 495 and clonidine, which are known to stimulate central dopamine (DA) and noradrenaline (NA) receptors respectively. Caffeine, but not pentobarbitone, markedly enhanced the reversal of the reserpine induced suppression of locomotor activity elicited by ET 495 + clonidine. Caffeine and pentobarbitone in combination were not more effective than caffeine alone in this respect. There were no obvious changes in the whole brain levels of NA and DA after treatment with caffeine or pentobarbitone or both. However, when combined, the two drugs caused a decreased disappearance of DA following inhibition of tyrosine hydroxylase by alpha-methyl-p-tyrosine. It is suggested that central catecholamine mechanisms are involved in the interaction between caffeine and barbiturates. 25 references. (Author abstract)

000252 Warsh, J. J.; Stancer, H. C. Clarke Institute of Psychiatry, Section on Neurochemistry, 250 College St., Toronto M5T 1R8, Canada **Brain and peripheral metabolism of 5-hydroxytryptophan-14C following peripheral decarboxylase inhibition.** Journal of Pharmacology and Experimental Therapeutics. 197(3):545-555, 1976.

The hypothesis that after selective peripheral decarboxylase inhibition, a greater fraction of peripherally measured monoamine metabolites should derive from central nervous system monoamine metabolism was examined. In rats pretreated with the peripheral decarboxylase inhibitor L-alpha-(3,4-dihydroxybenzyl)-alpha-hydrazinopropionic acid (MK-486) (50mg/kg i.p. or 50mg/kg i.v.), the peripheral formation of 5-hydroxytryptamine-14C (5-HT-14C) from the precursor DL-5-hydroxytryptophan-14C (5-HTP-14C) is reduced by 82-100% over a 4 hr interval. There is a marked increase in the penetration of 5-HTP-14C into brain and in the appearance in brain of 5-HT-14C and 5-hydroxyindoleacetic acid-14C (5-HIAA-14C). The cerebral metabolism of 5-HTP-14C in vehicle pretreated animals appears to occur mainly in the brain vascular compartment. Following MK-486 pretreatment, the in vivo metabolism of 14C-5-hydroxyindoles in the extracerebral compartment obeys linear kinetics as does the uptake and decarboxylation of 5-HTP-14C in brain. The cerebral turnover of 5-HT-14C appears to increase as a function of the dose of 5-HTP injected. This phenomenon may be a result of either saturation of brain 5-HT storage sites or nonspecific metabolism of 5-HTP in brain catecholamine neurons. A highly significant correlation is found between brain 5-HIAA-14C levels and blood 5-HIAA-14C levels following MK-486. The adrenal formation of 5-HT, which is not inhibited by MK-486, does not appear to contribute significantly to the blood 5-HIAA-14C levels. It is suggested that following peripheral decarboxylase inhibition, a larger fraction of peripherally measured 5-HIAA may derive

from central nervous system 5-HT metabolism. 51 references. (Author abstract modified)

000253 Weihrauch, T. R.; Rieger, H.; Kohler, H.; Voigt, R.; Hoffler, D.; Krieglstein, J. I. Medizinische Klinik und Poliklinik der Universitat, Langenbeckstr. 1, 6500 Mainz, West Germany **/Influence of diazepam and phenytoin on penicillin-induced cerebral convulsions./** Einfluss von Diazepam und Phenytoin auf durch Penicillin induzierte zerebrale Krampfanfalle. Arzneimittel-Forschung (Aulendorf). 26(3):379-382, 1976.

The effects of diazepam and phenytoin on penicillin induced EEG changes and convulsions were studied in 32 rabbits. EEG changes and convulsions were elicited by 2.4g/kg benzylpenicillin i.v. over 50 min. The dosages of the anticonvulsants were 1, 5 and 10mg of diazepam and 10, 10, and 30mg/kg of phenytoin. The qualitative and semiquantitative evaluation of the electroencephalograms revealed no reduction of spike frequency or spike amplitude for either of the two drugs. However, in contrast to phenytoin, diazepam was highly effective in preventing the development of generalized convulsions. None of the 12 diazepam treated animals developed a convulsion, whereas in most of the phenytoin treated animals and in most of the controls generalized convulsions appeared. The results suggest that diazepam should be used in the treatment of penicillin encephalopathy. 27 references. (Author abstract)

000254 Weinryb, I.; Michel, I. M. Dept. of Pharmacology, Squibb Inst. for Medical Research, Princeton, NJ 08540 **Amine-responsive adenylate cyclase activity from brain: comparisons between rat and rhesus monkey and demonstration of dopamine-stimulated adenylate cyclase in monkey neocortex.** Psychopharmacology Communications. 2(1):39-48, 1976.

The effects of biogenic amines on adenylate cyclase from rhesus monkey brain have been surveyed. Dopamine responsive cyclase activity was found throughout the subcortical limbic area and the limbic cortex, as well as in the sensorimotor cortex, where stimulation by dopamine was blocked by fluphenazine. Cyclase activity from caudate nucleus in rat and rhesus monkey was very similar in relative responsiveness to stimulation by dopamine and norepinephrine. Some response of the enzyme from cingulate and sensorimotor cortex to isoproterenol was observed. The inhibition from sensorimotor cortex raises the possibility of a cerebrocortical locus of action for antipsychotic agents. 14 references. (Author abstract)

000255 Werner, Toreen E.; Smith, Stanley G.; Davis, W. Marvin. Department of Pharmacology and Psychology, University of Mississippi, University, MS, 38677 **A dose-response comparison between methadone and morphine self-administration.** Psychopharmacology (Berlin). 47(2):209-211, 1976.

Rats were allowed to self-administer a solution of 0.9% saline, or 0.01, 0.03, 0.1, 0.3mg/kg/infusion of methadone hydrochloride or 0.03, 0.1or 0.3mg/kg/infusion of morphine sulfate. The results showed that number of infusions taken was an inverse function of unit dose, while amount of drug self-administered was a direct function of unit dose. The data also indicated that more morphine than methadone was self-administered. 11 references. (Author abstract)

000256 Westerink, Ben H. C.; Korf, Jakob. Laboratory for Pharmaceutical and Analytical Chemistry, Dept. of Clinical Chemistry, Antonius Deusinglaan 2, Groningen, The Netherlands **Turnover of acid dopamine metabolites in striatal and mesolimbic tissue of the rat brain.** European Journal of Pharmacology (Amsterdam). 37(2):249-255, 1976.

The disappearance of 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) from the brain of rats treated with pargyline and pargyline in combination with tropolone was studied. The DOPAC decline was exponential after pargyline treatment, while the HVA decline became a first order elimination when in addition to monoamine oxidase, catechol-O-methyl transferase was also inhibited. The turnover of the metabolites was calculated by multiplying the steady state level by the fractional rate constant (k). The data showed that under control conditions DOPAC is only partially O-methylated to HVA, while the formation of HVA via the methoxytyramine pathway is unlikely. DOPAC turnover, therefore, probably approximates dopamine turnover. 19 references. (Author abstract)

000257 Westfall, Thomas C.; Kitay, Deanna; Wahl, Georgia. Department of Pharmacology, University of Virginia Medical Center, Charlottesville, VA 22903 **The effect of cyclic nucleotides on the release of 3H-dopamine from rat striatal slices.** Journal of Pharmacology and Experimental Therapeutics. 199(1):149-157, 1976.

The effect of cyclic nucleotides on the release of monoamines from the central nervous system with isolated superfused striatal slices as a model was studied. The results indicate that 3H-dopamine (3H-DA) represents only a small proportion of the spontaneous overflow of radioactivity from superfused slices prelabeled with the amine, although 3H-DA represents the largest fraction recovered in the tissue. The results obtained provide direct support for the involvement of cyclic AMP in synaptic neurotransmission in the central nervous system. 30 references.

000258 Whishaw, Ian Q. Department of Psychology, University of Lethbridge, Lethbridge, Alberta, Canada **The effects of alcohol and atropine on EEG and behavior in the rabbit.** Psychopharmacology (Berlin). 48(1):83-90, 1976.

The effects of alcohol on the two types of cortical activation -- the movement related (atropine resistant) patterns and the immobility related (atropine sensitive) patterns -- are measured by changes in EEG activity in rabbits. Recordings were made from the hippocampus and neocortex. It was found that movement, movement related 6-12 Hz rhythmical slow activity (RSA), and movement related neocortical desynchronization were unaffected by intravenous atropine sulfate but depressed by ethyl alcohol (ethanol). Slower 4-8 Hz immobility related RSA and immobility related neocortical desynchronization produced by sensory stimulation (visual, auditory, tactile, vestibular) were relatively unaffected by ethanol even at high (0.1-0.2g%) blood alcohol levels, but were abolished by atropine sulfate. The results provide evidence for the idea of two pharmacologically separable cortical activating systems and suggest that ethanol has a greater effect on noncholinergic than cholinergic systems. 30 references. (Author abstract modified)

000259 Wiebel, Friedrich J.; Waters, Haywood L.; Elliot, Sandra; Gelboin, Harry V. Chemistry Branch, National Cancer Institute, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20014 **Effect of 7,8-benzoflavone on the duration of zoxazolamine paralysis and hexobarbital hypnosis in rats.** Biochemical Pharmacology (Oxford). 25(12):1431-1432, 1976.

The effect of 7,8-benzoflavone is reported on the duration of zoxazolamine paralysis and hexobarbital hypnosis times, both of which are functions of microsomal oxygenases. Male Sprague-Dawley rats were used; all compounds were given intraperitoneally. The laboratory animals were pretreated with

phenobarbital. The pretreatment of the rats decreases zoxazolamine paralysis times by 1/2 to 1/10, respectively, of the untreated animals. Injection of 7,8-benzoflavone shortly before the application of zoxazolamine has no significant effect on the paralysis time in control animals or on the change in paralysis caused by phenobarbital pretreatment. 21 references.

000260 Wilk, Sherwin; Glick, Stanley D. Department of Pharmacology, Mount Sinai School of Medicine of the City University of New York, Fifth Avenue and 100 St., New York, NY 10029 **Dopamine metabolism in the nucleus accumbens: the effect of clozapine.** European Journal of Pharmacology (Amsterdam). 37(1):203-206, 1976.

Dopamine metabolism in the nucleus accumbens of the rat was studied by gas chromatographic quantitation of 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA). The ratio of DOPAC/HVA in the nucleus accumbens is significantly greater than the same ratio in the striatum. Dose/response curves for the increase in DOPAC and HVA in the nucleus accumbens and striatum 2 hour after clozapine were generated. The effect of clozapine on dopamine metabolism is similar in both structures. It is concluded that the unique pharmacological profile of clozapine cannot be ascribed to a selective interaction of the drug with receptors of dopamine rich structures in the mesolimbic brain region. 10 references. (Author abstract modified)

000261 Wilkening, Doug; Mishra, Ram K.; Makman, Maynard H. Albert Einstein College of Medicine, Bronx, NY 10461 **Effects of morphine on dopamine-stimulated adenylate cyclase and on cyclic GMP formation in primate brain amygdaloid nucleus.** Life Sciences (Oxford). 19(8):1129-1137, 1976.

It is reported that in homogenates of Rhesus and Cebus monkey amygdaloid nuclear complex, adenylate cyclase activity was approximately doubled by either 10 microM dopamine or 8mM NaF. In the presence of morphine, the stimulation by dopamine was reduced. A 90% to 100% inhibition of the dopamine stimulation was obtained with 20 microM and a 50% inhibition with 5 microM morphine. The effects of 10 microM morphine on dopamine stimulation were reversed by 10 microM naloxone. Morphine itself did not significantly affect the basal adenylate cyclase activity, but in the presence of 10 microM morphine the stimulation by 8 microM NaF was reduced approximately 50%. Data suggest an action of morphine at a receptor site distinct from the dopamine receptor, but which inhibits the dopamine stimulated adenylate cyclase. In addition, the cyclic GMP content of Cebus amygdala slices was reduced by 50% to 75% during incubation for 5 to 20 minutes with morphine. Maximum effects on cyclic GMP were obtained with 10 microM, and half maximum effects with 0.1microM morphine. The effect of morphine on amygdala cyclic GMP was not reversed by naloxone. Thus, this action of morphine may not be receptor mediated, or may involve the interaction of morphine with receptors other than the opiate receptor. 35 references. (Journal abstract)

000262 Wise, Roy A. Center for Research on Drug Dependence, Department of Psychology, Concordia University, Montreal, Quebec, Canada **Evidence for involvement of a dopaminergic substrate in self-stimulation and intravenous amphetamine self-administration.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 205-207).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium, in April 1975, several lines of evidence which converge to suggest that a catecholaminergic system in the brain is critically involved in the rewarding effects of electrical brain stimulation and in the rewarding effects of intravenous amphetamine injections are analyzed to determine if these rewarding effects depend on a noradrenergic or dopaminergic mechanism, or both. Experiments are discussed in which the effects of dopaminergic receptor blockade using pimozide, alpha-noradrenergic blockade using phentolamine, and beta-noradrenergic blockade using propranolol on self-stimulation were studied using electrode placements in the paraventricular hypothalamus, the lateral hypothalamic portion of the medial forebrain bundle, and the substantia nigra pars compacta. Overall findings indicate that dopaminergic receptor blockade reduces the reward potency of amphetamine by interfering with neural mechanisms essential for reward perception. Such a view is considered compatible with the report that in humans dopamine receptor blockade reduces the euphoric effect of intravenous amphetamine. 6 references.

000263 Wong, David T.; Bymaster, Frank P. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Effect of nisoxetine on uptake of catecholamines in synaptosomes isolated from discrete regions of rat brain.** Biochemical Pharmacology (Oxford). 25(17):1979-1983, 1976.

The effects of nisoxetine, a potential antidepressant drug, on the uptake of radiolabeled norepinephrine by synaptosomes obtained from cerebral cortex, brain stem, hypothalamus and corpus striatum and on radiolabeled dopamine uptake by synaptosomes from corpus striatum and hypothalamus from rat brain was investigated. Nisoxetine inhibits the affinity uptake of norepinephrine by synaptosomes from hypothalamus, brain stem, and cerebral cortex of rat brain. The drug also inhibits the high affinity uptake of dopamine by hypothalamic synaptosomes. Nisoxetine has about 200 fold greater affinity for the uptake sites of norepinephrine than for those of dopamine. Nisoxetine administered intraperitoneally to rats reduces the high affinity uptake of catecholamines by synaptosomes of brain regions. A low affinity process for uptake of catechloamines also occurs in synaptosomes of hypothalamus, brain stem, and cerebral cortex but is not blocked by nisoxetine. The significance of the low affinity uptake processes is discussed. 16 references. (Author abstract modified)

000264 Woodruff, G. N.; Kelly, P. H.; Elkhawad, A. O. Department of Physiology and Biochemistry, University of Southampton, Southampton, England **Effects of dopamine receptor stimulants on locomotor activity of rats with electrolytic or 6-hydroxydopamine-induced lesions of the nucleus accumbens.** Psychopharmacology (Berlin). 47(2):195-198, 1976.

An experiment is presented in which ergometrine injected intraperitoneally into normal rats had little effect on locomotor activity. In contrast, rats with selective 6-hydroxydopamine induced lesions of dopamine terminals in the nucleus accumbens showed a strong stimulation of locomotor activity following injection of this dose of ergometrine. The dopamine analogue 2-amino-6-7-dihydroxy-1,2,3,4-tetrahydronaphthalene (ADTN) caused strong and long lasting stimulation of locomotor activity when injected intracerebroventricularly into rats. The ADTN response was markedly reduced in rats with bilateral electrolytic lesions of the nucleus accumbens, but unchanged in rats with bilateral electrolytic lesions of the caudate nucleus. At a lower dose level (50 micrograms) ADTN, injected intracerebroventricularly, had little effect on the locomotor activity of normal or sham operated rats. This dose of ADTN was, however, effective in causing locomotor stimulation of rats with bilateral 6-hydroxydopamine induced lesions

of the nucleus accumbens. These results support the view that the dopamine receptors in the nucleus accumbens are involved in the actions of locomotor stimulant drugs. 21 references. (Author abstract)

000265 Yates, Carol A.; Herbert, J. Dept. of Anatomy, University of Cambridge, Cambridge CB2 3DY, England **Differential circadian rhythms in pineal and hypothalamic 5-HT induced by artificial photoperiods or melatonin.** Nature (London). 262(5565):219-220, 1976.

Data were obtained on circadian rhythms in 5-hydroxytryptamine (5-HT) concentrations in various areas of the brain from ferrets kept for 8 weeks in either short days or long days; levels of 5-HT in the pineal and hypothalamus of ferrets kept in short photoperiods or long photoperiods after bilateral "decentralization" of the superior cervical ganglia; and levels of 5-HT in the pineal gland and hypothalamus of ferrets kept in long photoperiods and given either melatonin or arachis oil 8 hours after the start of the photoperiod. It was found that exposure of ferrets to either long photoperiods or short photoperiods induces differential 5-HT rhythms in the pineal and hypothalamus, which are abolished by autonomic denervation, and that melatonin induces 5-HT rhythms characteristic of animals kept in short photoperiods. It is suggested that differential 5-HT rhythms in thee pineal and hypothalamus could allow the animal's neuroendocrine system to discriminate between photoperiods which have the greatest significance for its reproductive function. 22 references.

000266 Yates, Celia M.; Wilson, Helen. MRC Brain Metabolism Unit, Department of Pharmacology, University of Edinburgh, Edinburgh EH8 9JZ, Scotland **Effect of chlorpromazine and acetylsalicylic acid in vivo on lysosomal enzymes in rat brain.** Brain Research (Amsterdam). 110(2):425-429, 1976.

The effects of chronic administration of chlorpromazine and acetylsalicylic acid on rat brain lysosomes were investigated. Test animals received 5mg of chlorpromazine hydrochloride daily, 5 days each week for 27 to 30 weeks by gastric tube; a 0.14mg/ml solution of chlorpromazine hydrochloride in drinking water daily for 31 to 33 weeks; or a 2.5mg/ml solution of acetylsalicylic acid in drinking water daily for 38 to 41 weeks. Administration of chlorpromazine in drinking water or by gastric tube has no effect on the specific activities, percent latencies and percent free/total activities of acid phosphatase, arylsulphatase and beta-galactosidase in either the striatum or occipital cortex when compared with controls. The protein concentrations of the striatum and occipital cortex are also unaffected by the chlorpromazine treatments. The protein concentrations and the specific activities, percent latencies and percent free/total activities of acid phosphatase, arylsulphatase and beta-galactosidase in rat striatum and occipital cortex are not significantly affected by the salicylate treatment. It is suggested that the enzymes studied are unlikely to be involved in the clinical effects of chlorpromazine. 11 references.

000267 Yokel, Robert A.; Wise, Roy A. Department of Pharmacology, University of Cincinnati Medical Center, 231 Bethesda Avenue, Cincinnati, OH 45267 **Attenuation of intravenous amphetamine reinforcement by central dopamine blockade in rats.** Psychopharmacology (Berlin). 48(3):311-318, 1976.

The roles of norepinephrine (NE) and dopamine (DA) in the reinforcing effects of stimulants were investigated in rats. DA receptor blockade by primozide or butaclamol caused periods of increased rate of responding for amphetamine self-administration which were followed, in the case of high doses, by response cessation. The response cessation produced by pimozide was not reversed by noncontingent amphetamine injections until well after the peak effect of the pimozide was over. When access to amphetamine was delayed until 4 hr after administration of pimozide, rate of responding was elevated. It is suggested that DA is critically involved in mediation of the reinforcing effects of amphetamine. Alpha adrenergic receptor blockade with phentolamine produced dose related decreases in responding; blockade with phenoxybenzamine had no effect. Beta adrenergic receptor blockade with levopropranolol decreased responding. The effects of phentolamine and propranolol do not appear to result from attenuation of the reinforcing effects of amphetamine. 37 references. (Author abstract modified)

000268 Yoshizaki, Toshio. Shionogi Research Laboratory, Shionogi & Co., Ltd., Fukushima-ku, Osaka, 553 Japan **Effects of cholinergic drugs and their blockers on adrenaline release from rat adrenal.** Biochemical Pharmacology (Oxford). 24(15):1401-1405, 1975.

Effects of cholinergic agents and their blockers on adrenaline secretion from rat adrenal were investigted. Nicotine induced adrenaline output was markedly prevented by hexamethonium. High doses of atropine also decreased nicotine induced adrenaline secretion from splanchnicotomized adrenal. Acetylcholine (ACh) subsequent to neostigmine caused marked secretion of adrenaline, which was almost completely blocked by atropine pretreatment. However, ACh induced adrenaline output from the splanchnicotomized adrenal was much less than that from the intact gland. The response of chronically and completely denervated adrenal to ACh was larger than that of the chronically or acutely splanchnicotomized gland. Pilocarpine increased adrenaline secretion and the output was prevented by pretreatment with atropine. In acutely splanchnicotomized rats, pilocarpine caused little increase of adrenaline secretion. Atropine caused a slight increase of adrenaline output in response to ether anesthesia, although methylatropine tended to inhibit output. Stimulation of the central end of the severed vagus at the cervical level had no effect on adrenaline liberation from splanchnicotomized adrenal with or without stimulation of splanchnic nerve. The sites of action of these drugs in rats are discussed. 18 references. (Journal abstract modified)

000269 Zemaitis, Michael A.; Greene, Frank E. Dept. of Pharmacology, School of Pharmacy, Univ. of Pittsburgh, Pittsburgh, PA 15261 **Impairment of hepatic microsomal drug metabolism in the rat during daily disulfiram administration.** Biochemical Pharmacology (Oxford). 25(12):1355-1360, 1976.

Male rats were given 0.1g/kg or 0.4g/kg of disulfiram (DS) daily by gavage for up to 12 days, in order to study the effects of chronic DS administration on hepatic microsomal drug metabolism. Administration of 0.4g/kg of DS resulted in significant impairment of aniline (ANL) hydroxylase after 1 day, but 2 days of DS treatment were required for significant inhibition of ethylmorphine (EtM) metabolism and depression of cytochrome P-450 levels. At this time, maximum impairment of ANL and EtM metabolism and maximum reduction of cytochrome P-450 levels were seen. Continued administration of DS for 10 additional days produced no further change in these parameters. ANL hydroxylase was also significantly reduced in treated animals throughout a 12 day period during which 0.1g/kg of DS was given. EtM N-demethylase activity and cytochrome P-450 levels were also reduced in animals so treated, but not until DS had been given for at least 5 days. However, by the end of the 12 day experimental period, EtM

metabolism and cytochrome p-450 levels had returned almost to control levels and only ANL hydroxylase was significantly different from control activity. Daily DS administration (0.4g/kg) produced small but significant increases in microsomal cytochrome b5 levels and in NADPH-cytochrome c reductase activity, whereas NADPH oxidase and NADPH-cytochrome P-450 reductase activities were significantly lower in treated rats. In addition to these effects in vivo, DS competitively inhibited EtM N-demethylase in vitro and bound to cytochrome P-450, producing a type I difference spectrum, thus providing additiona l mechanisms to account for impairment in vivo of drug metabolism by DS. 42 references. (Author abstract)

04 MECHANISM OF ACTION: BEHAVIORAL

000270 Adams, P. M.; Barratt, E. S. University of Texas Medical Branch, Galveston, TX 77550 **The effects of a marijuana extract on two-choice discrimination learning in the squirrel monkey.** Physiological Psychology. 4(2):155-158, 1976.

An experiment was conducted to determine the effects of delta9-tetracannabinol (THC), the primary psychoactive component of marijuana, on the acquisition of a two choice visual discrimination task involving either form or color cues. Eight adult male squirrel monkeys were pretrained to perform the discrimination task and their response time and accuracy of choice behavior was recorded. Four monkeys were then administered 0.68mg/kg THC 1 h before retesting trials. Discrimination accuracy on both dimensions was impaired by THC pretreatment. Response time was impaired on the first discrimination problem but evidence of tolerance development was present on the second. It is concluded that the acute effects of marijuana do produce a deficit in the ability of primates and subprimates to demonstrate acquisition of discriminations on both form and color dimensions. It is suggested that this deficit is partly the result of perceptual impairment, short-term memory impairment, and a general motor impairment which together impair the formation of a behavioral strategy appropriate for criterion performance. 21 references.

000271 Amit, Z.; Brown, Z. W.; Sklar, L. S. Center for Research on Drug Dependence, Concordia University, 1455 de Maisonneuve W., Montreal, Quebec, H3G 1M8 Canada **Intraventricular self-administration of morphine in naive laboratory rats.** Psychopharmacology (Berlin). 48(3):291-294, 1976.

The possibility that laboratory animals will self-administer morphine directly into the cerebral vesicles without shaping and without predependence was investigated in rats. Animals were neither predependent on morphine nor trained to press the operant lever. Experimental animals obtained intraventricular infusions of morphine through cannulae aimed at the left lateral cerebral ventricle. Control animals received only the vehicle and a third group of animals received equivalent but noncontingent morphine infusions. The mean number of lever presses per day was significantly higher for the experimental group than for the other group. Injections of naloxone at the termination of the experiment did not produce withdrawal symptoms indicating that the experimental animals were not physically dependent on morphine and were not self-administering the drug in order to relieve withdrawal symptoms. It is suggested that naive rats will work for the reinforcing properties of morphine when it is infused centrally. 26 references. (Author abstract modified)

000272 Ando, Kiyoshi. Department of Psychopharmacology, Central Institute for Experimental Animals, Kawasaki, Japan **Computer use in behavioral study.** Advances in Neurological Sciences (Tokyo). 19(6):1237-1244, 1975.

Ways of utilizing computer technology in behavioral research, both to analyze data and to control animal behavior in complex ways, are discussed. Two examples of computer applications to behavioral pharmacology and operant conditioning are reported. Measurements of interresponse time in the histograms of rats given psychotropic drugs (amphetamine, methamphetamine, pipradrol, and nicotine) was one of the applications. The other concerned the shaping of air sucking behavior in rhesus monkeys by a successive approximation technique by computer. New computer languages especially adaptable to behavior studies, such as SCAT, SDED, INTERACT, and FORTRAN, are discussed in their applications to behavioral science. It is concluded that the computer has become an indispensable tool to the behavioral psychologist, just as the microscope is to the biologist. 10 references. (Author abstract modified)

000273 Anlezark, Gill; Pycock, Chris; Meldrum, Brian. Dept. of Neurology, Institute of Psychiatry, Denmark Hill, London SE5 8AF, England **Ergot alkaloids as dopamine agonists: comparison in two rodent models.** European Journal of Pharmacology (Amsterdam). 37(2):295-302, 1976.

A series of ergot alkaloids, together with the dopamine (DA) agonists apomorphine and piribedil, was tested for protective effects against audiogenic seizures in an inbred strain of mice (DBA/2) and for induction of circling behavior in mice with unilateral destruction of one nigrostriatal DA pathway. The order of potency against audiogenic seizures was: apomorphine greater than ergocornine greater than bromocryptine greater than ergometrine greater than lysergic acid diethylamide (LSD) greater than methysergide greater than piribedil, while that observed in the rotating mouse model was apomorphine greater than ergometrine greater than ergocornine greater than bromocryptine greater than piribedil. LSD caused only weak circling behavior even when administered in high doses (greater than 1mg/kg). Methysergide was ineffective. Prior administration of the neuroleptic agent haloperidol blocked the effect of DA agonists and of ergot alkaloids in both animal models. The possible action of ergot alkaloids as DA agonists is discussed. 33 references. (Author abstract)

000274 Antelman, S. M.; Canfield, D. R.; Fisher, A. E. Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **The effect of dopamine-beta-hydroxylase inhibition on lateral hypothalamic self-stimulation and its facilitation by amphetamine.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p.187-190).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium, in April 1975, the effects of the dopamine-beta-hydroxylase (DBH) inhibitor, FLA-63, on lateral hypothalamic self-stimulation (LH/ICS) and the potentiation of LH/ICS by amphetamine are reported. FLA-63 produced significant depletion of norepinephrine in the cortex and hypothalamus as well as a 35% reduction of candate dopamine (DA) which is suggestive of an increase in DA turnover. Amphetamine markedly increased LH/ICS. In contrast to the depression of LH/ICS and elimination of amphetamine induced increases in responding reported by other investigators using other DBH inhibitors, FLA-63 had no effect on LH/ICS or on the amphetamine induced increases in responding. It is contended that these findings represent a strong challenge to any single catecholamine transmitter theory

of self-stimulation and suggest the neglected possibility of an interaction between NE and DA which is manifested by a compensatory increase in striatal DA turnover in the absence of NE. Whether or not this increase in DA turnover succeeds in maintaining or potentiating behavior would depend on the degree to which it is able to overcome antagonistic caudate influences. Action or behavioral stress would further increase striatal DA turnover, thereby maximizing the possibility of behavioral potentiation. 5 references.

000275 Areschka, Alex; Mahaux, Jean-Marie; Verbruggen, Francois; Houben, Christian; Descamps, Marcel; Broll, Madeleine; Werbenec, Jean-Pierre. Centre de Recherche de S. A. Labaz N. V., 1 avenue de Bejar, B-1120 Bruxelles, Belgium **/Research in the benzofuran series LVII. Benzofuryloxyalkylamidoximes: potential antidepressants./** Recherche dans la serie des benzofurannes LVII. Benzofuryloxyalkylamidoximes antidepresseurs potentiels. European Journal of Medicinal Chemistry (Paris). 10(4):398-407, 1975.

A series of benzofuryloxyalkylamidoximes were synthesized and the thymoanaleptic properties of these compounds were compared to the trycyclic antidepressant, imipramine. The properties of compounds 1 to 51 were submitted to tests relating to the noradrenergic, dopaminergic and serotoninergic systems. Results from these tests suggested the selection of compound 10 or L7526 for more thorough investigation. It was found that 1) the antireserpine properties of compound 10 were four times superior to those of imipramine; 2) L7526 highly potentializes the phenomenon of group toxicity under amphetamines whereas imipramine has no effect; 3) there was no significant monoamine oxidase inhibitor activity; 4) compound 10 manifested high antagonist activity in relation to the tremorine and was superior to imipramine. 15 references.

000276 Areschka, Alex; Mahaux, Jean-Marie; Verbruggen, Francois; Houben, Christian; Descamps, Marcel; Werbenec, Jean-Pierre; Broll, Madeleine. Centre de Recherche de S. A. Labaz N. V., 1, avenue de Bejar, B-1120 Bruxelles, Belgium **/Aryloxyalkyl amidoximes: potential antiaggressives./** Aryloxyalkylamidoximes a potentialites antiagressives. European Journal of Medicinal Chemistry (Paris). 10(5):463-469, 1975.

A series of aryloxyalkyl amidoximes were prepared in order to study their thymoanaleptic activity. General properties of various compounds were examined in relation to their effect on the noradrenergic, dopaminergic and serotinergic systems of rats and mice. Special attention was given to the compound 2-(1-naphthyloxy)-propionamidoxime of L-7600. It was found that L-7600 exhibits a powerful inhibitory effect on aggressivity and acts more intensively on the psychic factors of behavior than on the motor factors. 9 references.

000277 Babbini, M.; Gaiardi, M.; Bartoletti, M. Institute of Pharmacology, University of Bologna, Via Irnerio 48, I-40126 Bologna, Italy **Effects of combined treatment with nortriptilene and lorazepam on conflict behavior and motility of rats.** Psychopharmacology (Berlin). 48(3):251-254, 1976.

The effects of nortriptyline and lorazepam, alone and in combination, on the response rate in the multiple schedule of reinforcement procedure devised by Geller and Seifter (1960) and on motor activity were studied in rats. Lorazepam attenuated the suppressant effects of punishment on the response rate of rats in the multiple schedule of reinforcement. Nortriptyline alone was ineffective on punished responses. Both drugs responding inhibited the nonpunished response. Combined treatment with the two drugs attenuated the effects punishment at all dose levels tested. The effects of the combination upon both punished responding and nonpunished responding was greater than might be accounted for by a simple additive effect of the individual treatments. Lorazepam and nortriptyline each induced a dose related decrease in the locomotor activity of rats; when given together the drugs antagonized each other. The results give no experimental support to clinical observations about the usefulness of the benzodiazepine antidepressant combination in certain depressive illnesses. 20 references. (Author abstract modified)

000278 Baldessarini, R. J.; Walton, K. G.; Borgman, R. J. Psychiatric Research Laboratories, Massachusetts General Hospital, Boston, MA 02114 **Prolonged apomorphine-like behavioural effects of apomorphine esters.** Neuropharmacology (Oxford). 15(8):471-478, 1976.

The activities of a series of esters of apomorphine including diacetylapomorphine, dipropionylapomorphine, diisobutrylapomorphine, dipivaloylapomorphine and dibenzoylapomorphine were studied in vivo in the rat and in vitro using striatal homogenates. All esters provoked stereotyped gnawing behavior in intact rats, as well as rotation in a direction contralateral to unilateral electrolytic lesions in the nigrostriatal pathway. The esters were somewhat less potent than apomorphine in inducing these behavioral responses, and had a delayed latency to maximal effect as well as a prolonged duration of action. Prolongation of the behavioral effects of the esters increased with the size of the ester substituent. Acute intraperitoneal doses of all esters, up to 100mg/kg, were well tolerated. The behavioral activity of the esters after intragastric administration was poor. None of these esters increased the synthesis of cyclic AMP in striatal homogenates exhibiting adenylate cyclase activity stimulated by apomorphine or dopamine, and the smaller esters appeared to inhibit stimulation by dopamine. It is concluded that the desirable prolongation of action of labile esteric derivatives of apomorphine is probably due to their increased lipophilic properties or to slow hydrolysis of the larger esters that converts the depot pro-drugs to the probable active product, apomorphine. 41 references. (Author abstract modified)

000279 Baldessarini, Ross J.; Griffith, Fred F. Psychiatric Research Laboratories, Department of Psychiatry, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114 **Acute increases by p-chlorophenylalanine of apomorphine-induced stereotyped behavior in the rat.** Psychopharmacology (Berlin). 48(1):91-95, 1975.

An investigation of the potentiation of apomorphine induced stereotyped gnawing behavior in the rat by p-chlorophenylalanine (PCPA) was conducted. The potentiation effect was dependent on the dose of PCPA and half maximal at approximately 150mg/kg, i.p.;it occurred within 30 min, was greatest between 1 and 5 h and had nearly disappeared by 24 h after an acute dose of PCPA. A similar effect was not found at 24 or 48 h following 3 repeated doses of PCPA of 300mg/kg day. This effect of PCPA was not reversed by 5-hydroxytrytophan (5-HT) or by high doses of a decarboxylase inhibitor. PCPA alone did not produce sterotyped behavior, although it produced some behavioral excitation in high doses following inhibition of monoamine oxidase. This acute behavioral effect of PCPA to potentiate apomorphine induced stereotyped responses is unexplained. It does not seem to be due to depletion of 5-HT or to the formation of an amine as an active metabolite. It is suggested that PCPA can have behavioral excitatory actions independent of its 5-HT depleting action. 18 references. (Author abstract modified)

000280 Barr, Gordon A.; Gibbons, Judith L.; Bridger, Wagner H. Department of Psychiatry, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461 **Neuropharmacological regulation of mousekilling by rats.** Behavioral Biology. 17(2):143-159, 1976.

The literature concerning the neuropharmacology of mouse killing (muricide) is reviewed with attention to the behavioral specificity of the response. Several tentative conclusions are forwarded: 1) increases in monoamine activity (serotonin or catecholamine) result in a behaviorally specific blockade of the killing response in natural killers; and 2) large decreases in brain serotonin by peripheral or central drug treatment or by central brain lesions induce killing in both naive rats and experienced nonkiller rats. The mode of depletion is important and, with certain manipulations, the induction of killing is accompanied by increases in general irritability and by an alteration of the stereotypic killing pattern. Large depletions of the catecholamines either by synthesis inhibition or by neurotoxic drug action did not induce killing in the majority of nonkillers. Peripherally administered cholinergic agonists and antagonists, with two exceptions, were ineffective in inducing killing in nonkillers or in blocking killing by killers. Evidence for centrally elicited stereotyped killing by cholinergeric stimulation of brain tissue is not consistent, but cholinergic systems are implicated in the facilitation of killing by spontaneous killers. 74 refererences. (Author abstract)

000281 Barratt, E. S.; Adams, P. M.; Poffenbarger, P. L.; Fritz, R. R.; Abell, C. W. Behavioral Science Lab., University of Texas Medical Branch, Galveston, TX 77550 **Effects of rapid depletion of phenylalanine and tyrosine on sleep and behavior.** Pharmacology Biochemistry and Behavior. 5(1):47-53, 1976.

Plasma phenylalanine (PHE) and tyrosine (TYR) were rapidly lowered to trace levels within 4 hours by intraperitoneal administration of phenylaline ammonialyase (PAL), an enzyme which specifically deaminates both PHE and TYR to inactive products, in a study of the effects of fluctuations of free amino acid concentrations in plasma on sleep patterns and operant behavior in the squirrel monkey. Significant alterations in sleep patterns and in performance on a chained operant task involving hold and reaction time components were found, but no significant effect on the performance of a simple operant task was observed. Administration of saline or trans-p-cinnamic acid and trans-p-coumaric acid, the products of PHE and TYR deamination, produced no changes in behavior or sleep patterns. The reduction of plasma PHE and TYR resulted in a significant decrease in PHE and TYR levels in whole rat brain. Brain serotonin levels were increased within 4 h after PAL administration, whereas, dopamine and norepinephrine levels were decreased subsequently (within 8 hr). These studies suggest that circulating levels of PHE and TYR are involved directly or indirectly in the modulation of certain parameters of brain function. 31 references. (Author abstract)

000282 Barry, Herbert, III. University of Pittsburgh, Pittsburgh, PA **Behavior and drug effects during chronic stress.** Psychopharmacology Bulletin. 12(3):76, 1976.

A series of experiments is conducted to test the joint effects of drugs and physical stress on physiology and behavior. The development of drug tolerance, influence on seizure susceptibility and impact on arousal are also studied. Tetrahydrocannabinol (THC) decreases the aggressiveness of a dominant rat toward a subordinate but administration of THC to the subordinate rat impairs its defensive behavior and increases aggression on the part of the dominant rat. Alcohol administered to a subordinate rat inexperienced in fighting causes the subordinate rat to be more readily victimized and wounded by a dominant rat; however, this does not occur with subordinate rats who are experienced in fighting. Other reported effects of THC are: 1) an anticonvulsant effect more similar to that of diphenythydantoin than to that of pentobarbital or chlordiazepoxide; 2) a sedative action similar to pentobarbital and chlordiazepoxide; 3) an analgesic effect which is enhanced by pretreatment with SKF-525A, a metabolic inhibitor; 4) a shortening of the sleeping time induced by zoxazolamine and hexobarbital; and 5) a prolongation of barbital induced sleeping time. Bemegride and pentylenetetrazol reverse the responses in animals trained to discriminate pentobarbital from saline or pentobarbital from alcohol. In another series of tests, animals trained to discriminate chlorpromazine (CPZ) from saline were administered a number of CPZ metabolitic. The centrally active metabolite 7-hydroxy-CPZ elicits the drug response; inactive or peripherally active metabolites do not. It is suggested that the discriminative stimulus is based on the effects of a drug on the central nervous system.

000283 Bartus, Raymond T.; Johnson, H. R. Psychopharmacology, Park-Davis Research Laboratories, Ann Arbor, MI 48106 **Short-term memory in the Rhesus monkey: disruption from the anti-cholinergic scopolamine.** Pharmacology Biochemistry and Behavior. 5(1):39-46, 1976.

Two separate experiments were conducted on adolescent male Rhesus monkeys to evaluate the effects of the anticholinergic scopolamine on primate visual discrimination and short-term memory (STM). The results on the first experiment confirm that relatively mild doses of scopolamine profoundly impair visual discrimination performance. This severe impairment, at doses producing few overt effects, suggests a direct effect on discrimination mechanisms. Therefore, tests designed to evaluate the role of acetycholine in other behavioral processes, such as STM, should control for this confounding, debilitating influence on visual discrimination when anticholinergic agents are used. The results of the second experiment demonstrate a clear interaction between the effects of an anticholinergic and the length of the retention interval. This interaction provides evidence that one specific result of cholinergic blockade is the impairment of performance in situations where information must be held in memory for short periods of time. On the basis of these data, it seems reasonable to conclude that acetylcholine is not only involved in the acquisition and long-term retrieval of newly learned habits, but is also intimately involved in the expression of primate STM as well. 30 references. (Author abstract modified)

000284 Baturin, V. A. Kafedra farmakologii, Meditsinskogo Instituta, Chita, USSR **/Effect of psychostimulants on rats' relearning of the direction of avoidance in a U-maze./** Vliyaniye psikhostimulyatorov na pereobucheniye krys napravleniyu izbeganiya v u-obraznom labirinte. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 81(5):554-556, 1976.

Because previous studies had shown that partial destruction of cerebral stria led to destruction of relearning of the direction of avoidance in the rat, a study was made of the effects of various doses of fenamine (d,l-amphetamine) and of caffeine on relearning of the direction of avoidance in a U-maze. The experiment was performed with 144 white rats, given 0.5mg/kg, 2mg/kg, or 5mg/kg fenamine or 25mg/kg or 50mg/kg caffeine. Results showed the lower doses of fenamine shortened the latent periods of response but failed to affect relearning, and the high dose reduced latency and inhibited

reconstruction of the learned avoidance. Neither dose of caffeine produced an effect on relearning. 7 references.

000285 Baxter, M. G.; Leach, M. J.; Miller, A. A.; Sethna, D. M.; Wheatley, P. L. Pharmacology Laboratory, Wellcome Research Laboratories, Beckenham, Kent BR3 3BS, England **Some behavioural and EEG studies on the behavioural depression in induced in the rat by ethanolamine O-sulphate, an inhibitor of GABA-transaminase.** British Journal of Pharmacology (Basingstoke). 57(3):431P, 1976.

The behavioral depression produced in rats by elevation of whole brain concentration of GABA resulting from intraventricular injection of ethanolamine O-sulfate (EOS) was compared with that produced by subcutaneously injected chlorpromazine (CPZ). Brain GABA concentration is elevated significantly by EOS in doses ranging from 160ug to 320ug. CPZ administered 1 hour prior to observation completely antagonizes the gnawing induced by apomorphine administered 30 minutes prior to observation; EOS in doses of 240ug and 320ug administered 24 hours previously does not antagonize the gnawing. In the shock avoidance conditioning test using training rats, mean hourly response latencies are significantly increased at 5 hours, 24 hours, and 48 hours by 200ug and 240ug doses of EOS but not by 160ug of EOS. CPZ significantly increases response latency at 1 hour, 3 hours, and 5 hours after administration. This test does not reveal obvious relationship between elevated brain GABA concentration and behavioral depression. EEG studies were performed in which the parietal EEG, recorded on magnetic tape, was analyzed by passing it through four broad wave band filters which measured the voltage within each of the following frequencies: 2.4Hz to 4.0Hz, 4.0Hz to 7.5Hz, 7.5Hz to 13.5Hz, and 13.5Hz to 26.0Hz filters 1 to 4 respectively. CPZ significantly increases voltages in Filters 1 and 2 and total voltage at all times, but voltages in Filter 3 and Filter 4 are significantly increased at 1 hour to 4 hours and 2 hours to 4 hours respectively. EOS significantly increases total voltage and voltage in Filter 1, Fi lter 2 and Filter 3 at 24 hours and 48 hours. It is concluded that the behavioral depression associated with increased brain GABA concentrations induced by EOS in rats differs from depression induced by CPZ in some important respects. 5 references.

000286 Beck, Sidney L.; Gavin, Donna L. Dept. of Biology, Wheaton College, Norton, MA 02766 **Susceptibility of mice to audiogenic seizures is increased by handling their dams during gestation.** Science. 193(4251):427-428, 1976.

Pregnant mice were handled and given injections of 50 milligrams of beta-2-thienylalanine, solvent or a sham injection on days 10, 11 and 12 of gestation, and the pups were tested for susceptibility to audiogenic seizures 23 days after birth. Pups from all mothers had identical frequencies of audiogenic seizures, and these frequencies were significantly higher than those of an unhandled control group. Results of the sham treatment suggests that maternal stress induced by handling, rather than the nature of the substance injected, increased the susceptibility of the offspring to seizures. 14 references. (Author abstract)

000287 Berry, P. A. Pharmaceutical Research, Nottingham, England **Anxiety drugs and baboon behaviour.** Bulletin of the British Psychological Society (London). 28:223, 1975.

Using suppression of aggressive behavior as an index of anxiolytic activity, three simple methods for detecting antianxiety agents were explored in a small colony of baboons. The importance of developing methods of evaluation that are related to the eventual use of the substance, particularly in the case of antianxiety drugs, is emphasized. Findings indicated that human intrusion into the primate colony proved to be most effective and reproducible means of inducing aggression within the group. A very close correlation between the minimal dose of antianxiety agent required to suppress the aggressive behavior of the leader of the colony and the daily recommended human therapeutic dose was established. In all cases the minimal effective dose levels of drugs used were close to those recommended for humans. 2 references. (Author abstract modified)

000288 Bignami, Giorgio. Istituto Superiore di Sanita, Viale Regina Elena 299, I-00161 Roma, Italy **Nonassociative explanations of behavioral changes induced by central cholinergic drugs.** Acta Neurobiologiae Experimentalis (Warszawa). 36(1/2,B):5-90, 1976.

Studies concerning effects of cholinergic stimulants and blockers on habituation, alternation, classical and instrumental conditioning, differentiation and discrimination are summarized and discussed. The analysis suggests that results originally ascribed to associative changes can be accounted for by nonassociative factors inherent in the experiments. The data also show that neither one of the more economical nonassociative explanations at either the sensory, drive or response level can by itself account for the interactions observed. Studies dealing with drug (atropine, scopalamine, physostigmine, d-amphetamine) effects in lesioned animals and those using intracerebral treatments, point out several sites of action of muscarinic agonists and antagonists in the septum, hippocampus, amygdala, striatum, hypothalamus, midline thalamic nuclei and reticular formation. It is provisionally concluded that central muscarinic systems subserve several functions, ranging from modulation of consummatory responses to control of motor act differentiation. Both drug and lesion studies show not only that the frontolimbic system has a considerable role in the latter process, but also that localization of motor act differentiation under a given drive depends both on the category of the cue and on the category of the response. Some comparisons between the effects of muscarinic agonists and blockers and those of other drugs indicate that the alteration of sensory/motor relations caused by the former can be separated by motor hyperactivity, selective response enhancements caused by the indole hallucinogen LSD-25, attenuation of punishment suppression by benzodiazepines and subhypnotic doses of barbiturates and hyperarousal or hyperreactivity syndrome induced by compounds which deplete central 5-hydroxytryptamine. 339 references. (Journal abstract modified)

000289 Bloom, Alan S.; Dewey, William L.; Harris, Louis S.; Brosius, Keith K. Department of Pharmacology, Box 726 MCV Station, Richmond, VA 23298 **The correlation between antinociceptive activity of narcotics and their antagonists as measured in the mouse tali-flick test and increased synthesis of brain catecholamines.** Journal of Pharmacology and Experimental Therapeutics. 198(1):33-41, 1976.

The effects of several narcotics, narcotic antagonists/analgesics and narcotic antagonists on the synthesis of dopamine and norepinephrine in mouse brain were estimated and related to their activity in the tail- flick test. Catecholamine synthesis was estimated by measuring the accumulation of 3H-dopamine and 3H-norepinephrine formed from an injection of 3H-tyrosine. Morphine produced dose related increases in both tail-flick activity and catecholamine synthesis. Each of the narcotic analgesics produced a significant increase in catecholamine synthesis 30 min after the subcutane-

ous injection of an antinociceptive dose. Under these same conditions, drugs which are inactive in the tail-flick test, such as pentazocine, produced a decrease in catecholamine synthesis and cyclazocine: naloxone and naltrexone were without significant effect. However, cyclazocine, which was inactive in the tail-flick test and did not alter catecholamine synthesis 30 min after administration, demonstrated tail-flick activity and produced increased catecholamine synthesis 2 min after its adminstration. Morphine was devoid of either activity 2 min after administration. Similarly, at 2 hours after the administration of a dose of morphine that was active in the tail-flick test and increased catecholamine synthesis at 30 min, neither tail-flick activity nor increased catecholamine synthesis was observed. Naloxone blocked both the antinociceptive action and the increased catecholamine synthesis produced by both morphine and methadone. Results indicate that a correlation exists between tail-flick activity of narcotic-like drugs and their ability to increase catecholamine synthesis. The hypothesis that brain catecholamines may be involved in the central mediation of the tail-flick response and other actions of the narcotic analgesics is supported. 35 references. (Author abstract)

000290 Blundell, Carole; Crossman, A. R.; Slater, P. Departments of Physiology and Anatomy, University of Manchester, England **The effect of morphine on turning behaviour in rats and mice with unilateral 6-hydroxydopamine lesions.** British Journal of Pharmacology (Basingstoke). 57(3):456P, 1976.

The effect of morphine on turning induced by dextroamphetamine or apomorphine was studied in rats with unilateral lesions of the substantia nigra induced by injection of 6-hydroxydopamine (6-OHDA). The mean turning rate recorded after amphetamine injection is reduced by 45% when 2mg/kg of morphine is administred along with the dextroamphetamine. Apomorphine induced turning is not affected by 2mg/kg of morphine but is reduced by 18% following 4mg/kg of morphine. The effects of morphine on turning induced by dextroamphetamine was also studied in rats and in mice with unilateral lesions of the left striatum induced by injection of 6-OHDA. In rats, 4mg/kg of morphine reduces the dextroamphetamine induced mean turning rate by 71%; 8mg/kg doses of morphine stop the destroamphetamine induced turning completely. The reduction by morphine of dextroamphetamine induced turning is entirely prevented by naloxone. Levorphanol totally suppresses dextroamphetamine induced turning but dextrorphan does not. In mice, 4mg/kg of morphine has no effect on dextroamphetamine induced turning. It is concluded that the results are consistent with the hypothesis of Kuschinsky and Hornykiewicz (1974) that one effect morphine in the rat is to reduce the release of dopamine in the striatum but that morphine does not apparently have the same action in the mouse. 3 references.

000291 Blundell, J. E.; Latham, C. J.; Leshem, M. B. Psychology Department, University of Leeds, Leeds LS2 9JT, England **Differences between the anorexic actions of amphetamine and fenfluramine -- possible effects on hunger and satiety.** Journal of Pharmacy and Pharmacology (London). 28(6):471-477, 1976.

The inhibition of feeding in rats brought about by amphetamine and fenfluramine was continuously monitored for periods up to 24 hrs using a pellet detecting eatometer. For rats tested under conditions of food deprivation, the two drugs gave rise to distinctive anorexic profiles: amphetamine delayed the onset of eating whereas fenfluramine allowed eating to commence normally but brought about an early termination of the initial bout of feeding. When the drugs were administered to rats with free access to food, analysis of the meal pattern showed that amphetamine gave rise to a small increase in the intermeal interval while fenfluramine brought about a clear reduction in meal size. It is suggested that the contrasting modes of action of these drugs represent an effect of amphetamine upon hunger and an action of fenfluramine on satiety. This suggestion is in keeping with the proposed mechanisms of action of these drugs, amphetamine acting upon a hypothalamic motivational system and fenfluramine acting by means of a postulated serotoninergic satiety system. Use of the continous monitoring technique has pointed to certain limitations in the assessment of anorexic drug action by means of discrete food sampling periods. 29 references. (Author abstract)

000292 Boucsein, Wolfram; Wendt-Suhl, Gitta. Fachbereich 2: Psychologie, Gesamthochschule, Lotharstrasse 65, D-4100 Duisburg, Germany **The effect of chlordiazepoxide on the anticipation of electric shocks.** Psychopharmacology (Berlin). 48(3):303-306, 1976.

The effect of chlordiazepoxide in two anxiety evoking conditions and a control condition was investigated in human subjects. Subjects were told to expect an electric shock twice as strong or five times as strong as a shock they had previously found unpleasant. The control group was told to expect a questionnaire rather than a shock. During a 20 min anticipation interval, heartrate, galvanic skin reaction, and a rating of subjective emotional arousal were continously recorded. under the strong stress condition chlordiazepoxide had an anxiety reducing effect. However, in the control group and to some extent in the weak stress condition, chlorpromazine produced more anxiety than did the placebo. 11 references. (Author abstract modified)

000293 Broekkamp, C. L. E. Department of Pharmacology, University of Nijmegen, Nijmegen, The Netherlands **The effects of manipulations with the dopaminergic system on self-stimulation behavior.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 194-195).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium, in April 1975, results are given from a study of the effects of pharmacological manipulation with apomorphine, d-amphetamine, and haloperidol on self-stimulation behavior in rats. Apomorphine, a specific dopamine receptor stimulant, was reinforcing, and the effect appeared responsible for engagement in stereotyped behavior that was shaped into stereotyped lever pressing in about half of the animals. Bilateral injections of d-amphetamine into the neostriatum tended to depress self-stimulation, whereas unilateral injections into the nucleus accumbens increased lever pressing rate. Bilateral injections into the nucleus accumbens enhanced lever pressing rate much more effectively. Application of the dopamine blocking agent haloperidol into the neostriatum both unilaterally and bilaterally again indicated the effectiveness of bilaternal injections. Overall findings agree with the hypothesis involving the dopaminergic system in mediation of reward, but do not actually prove such mediation. Rather it is shown that the motivation for self-stimulation behavior is also mediated by the dopaminergic system, and a theoretical model for self-stimulation behavior should therefore indicate that the same pathway mediates both reinforcement and motivation.

000294 Carrer, Hugo; Meyerson, Bengt J. Department of Medical Pharmacology, Biomedicum, Box 573, S-75123 Upp-

sala, Sweden **Effect of CNS depressants and stimulants on latency for appearance of copulatory response in the female rat.** Pharmacology Biochemistry and Behavior. 4(5):497-505, 1976.

The effect of several psychoactive drugs on the time required for endogenously released progestin to activate the lordosis response was studied in rats. Diethyl ether anesthesia, sodium hexobarbital (20mg/kg), diphenylhydantoin (50mg/kg), strychnine (1mg/kg), and picrotoxin (1-0.25mg/kg) effectively induced the copulatory response (lordotic behavior) in estradiol benzoate treated ovariectomized rats although no progesterone was given. As none of the tested compounds were effective in replacing progesterone in adrenalectomized animals, adrenal secretion is likely to be implicated in the lordosis activating effect of these compounds. The lordosis response appeared faster after the CNS stimulants than after treatment with the CNS depressants. The influence of diethylether anesthesia, strychnine (0.5mg/kg) or picrotoxin (0.25mg/kg) on the latency for the appearance of the lordosis response after IV injection of isopregnenone was studied in estradiol benzoate treated ovariectomized females. A 10 min ether anesthesia delayed the onset of the lordosis response in adrenal intact as well as adrenalectomized animals. Anesthesia given after receptivity had been fully established suppressed the responses for a short period (10-30 min) after the narcosis. The delay of the appearance of the first lordosis response after IV injection of isopregnone exceeded this period. Strychnine but not picrotoxin significantly shortened the latency to the onset of the female copulatory response. It is concluded that the lordotic activating action of progesterone or steroids with progesteronelike ability released from an endogenous source or given IV is influenced by compounds which exert a depressant or stimulant effect on neuronal activity. The total response obtained is not changed but the appearance of the response is prolonged by CNS depressants and shortened by certain CNS stimulants. 34 references. (Author abstract modified)

000295 Carter, Richard B.; Appel, James B. Behavioral Pharmacology Laboratory, Department of Psychology, University of South Carolina, Columbia, SC 29208 **Blockade of the behavioral effects of 5-HTP by the decarboxylase inhibitor Ro 4-4602.** Pharmacology, Biochemistry and Behavior. 4(4):407-409, 1976.

Twenty male rats were trained to press a bar on a fixed-ratio (FR 32) schedule of water reinforcement. The behavioral effects of 5-hydroxytryptophan (5-HTP) (50mg/kg) were studied following pretreatment with small (50mg/kg) and large (400mg/kg) doses of the decarboxylase inhibitor Ro 4-4602. It was found that both doses of the pretreatment agent blocked the disruptive effects of 5-HTP. This result suggests that at least some of the effects of 5-HTP may be mediated peripherally. 11 references. (Author abstract)

000296 Castellano, Claudio. Laboratorio di Psicobiologia e Psicofarmacologia, C. N. R., via Reno 1, I-00198 Roma, Italy **Effects of caffeine on discrimination learning, consolidation, and learned behavior in mice.** Psychopharmacology (Berlin). 48(3):255-260, 1976.

The effects of caffeine were investigated in a series of experiments carred out in a Y watermaze in which mice were required to swim toward a light source (L procedure), corresponding to natural preference, or toward the dark (D procedure), corresponding to the acquisition of a new pattern of behavior. Caffeine administration to naive animals facilitates the learning process and the consolidation process in the D procedure and improves the natural tendencies in the L procedure. In mice pretrained in the D procedure, caffeine administration disrupts the acquired behavior. In mice pretrained in the L procedure, only very high doses of caffeine produce disruption of performance. 32 references. (Author abstract modified)

000297 Castellano, Claudio. Laboratorio di Psicobiologia e Psicofarmacologia del Consiglio Nazionale delle Ricerche, Via Reno 1, I-00198 Rome, Italy **Effects of nicotine on discrimination learning, consolidation and learned behaviour in two inbred strains of mice.** Psychopharmacology (Berlin). 48(1):37-43, 1976.

The effects of nicotine on discrimination learning, consolidation and learned behavior are investigated in two inbred strains of mice which were shown to differ both in learning abilities and in brain chemistry. DBA/2J and C57BL/6J mice were injected with nicotine and tested in water Y-maze in two procedures: the L-procedure, corresponding to innate behavior, in which the animals must swim towards the light, and the D-procedure, corresponding to the acquisition of a new pattern of behavior, in which they must swim toward the dark. Three sets of experiments were carried out: 1) in the pretrial experiments, nicotine administration improved the innate tendencies of both strains, while the acquisition of new behavior was facilitated in the C57 and impaired in the DBA mice, 2) in the posttrial experiments (D-procedure), nicotine administration induced clear facilitating effects on the consolidation processes of the C57, while impairing these processes in DBA strain, 3) the only effect evident, following nicotine administration, before the highest doses were reached, in the trained mice of both strains, was a performance impairment of the DBA mice trained in the L-procedure. 27 references. (Author abstract modified)

000298 Collier, H. O. J.; Hammond, M. D.; Schneider, C. Miles Laboratories Limited, Stoke Poges, Slough, SL2 4LY, England **Effects of drugs affecting endogenous amines or cyclic nucleotides on ethanol withdrawal head twitches in mice.** British Journal of Pharmacology (London). 58(1):9-16, 1976.

The hypothesis that head twitching in mice can be used as an indicator of ethanol withdrawal is examined. Twenty four hr after ethanol withdrawal, dependent mice exhibited frequent head twitching. Naive mice exhibited similar twitching 15 min after treatment with 5-hydroxytryptophan (5-HTP) or 6 h after alpha-methyl-p-tyrosine (AMPT). Ethanol lessened the incidence of head twitches induced by any of these treatments. 5-HTP and AMPT each increased the incidence of head twitches induced by withdrawal of ethanol from dependent mice. Drugs that affect the amount or activity of endogenous amines or cyclic mucleotides modified the incidence of head twitches. Nearly all drugs acted in the same direction on twitching elicited by any of these three treatments. It is concluded that the findings suggest that head twitching induced by these three treatments arises from a common biochemical mechanism, which may ultimately be a change in favor of cyclic GMP of the balance between this nucleotide and cyclic AMP within appropriate neurones. This imbalance appears to be elicited or increased by 5-hydroxytryptamine and acetylcholine and to be decreased by dopamine, noradrenaline and E prostaglandins. 36 references. (Author abstract modified)

000299 Colpaert, Francis C.; Desmedt, Luc K. C.; Janssen, Paul A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Discriminative stimulus properties of benzodiazepines, barbiturates**

and pharmacologically related drugs; relation to some intrinsic and anticonvulsant effects. European Journal of Pharmacology (Amsterdam). 37(1):113-123, 1976.

Using a food reinforced, two lever operant method, 12 rats were trained to discriminate between orally administered chlordiazepoxide and orally administered solvent. The rats were then used in generalization experiments with various benzodiazepines (bromazepam, diazepam, flurazepam, lorazepam, nitrazepam, and oxazepam), barbiturates and related compunds (pentobarbital, phenobarbital, glutethimide, thalidomide, and baclofen), and neuroleptic drugs (haloperidol and chlorpromazine). The ability of these drugs to induce a discriminative stimulus complex similar to that induced by chlordiazepoxide was then compared with some intrinsic and anticonvulsant effects of the same drugs. The discriminative stimulus properties of benzodiazepines, barbiturates, and related compounds correlate with the ability of these drugs to induce ataxia, as well as with part of their anticonvulsant activity. Haloperidol and chlorpromazine do not produce the chlordiazepoxide discriminative stimulus complex. The stimulus properties of these drugs, as defined by the procedure described, are based neither on their ataxia inducing effect, nor on their general depressant or sedative action. It is concluded that these properties constitute a pharmacologically, but not a chemically highly specific phenomenon. 23 references. (Author abstract modified)

000300 Cooper, Barrett R.; Breese, G. R. Dept. of Psychiatry and Pharmacology, Univ. of North Carolina School of Medicine, Chapel Hill, NC 27514 **A role for dopamine in the psychopharmacology of electrical self-stimulation.** In: Bernard, B., Aminergic hypotheses of behavior: reality or cliche? Rockville, MD, National Institute on Drug Abuse, 1975. 149 p. (p. 63-70).

The psychopharmacology of electrical self-stimulation of the lateral hypothalamus was studied using 6-hydroxydopamine, alpha-methyltyrosine, U-14,624, and d-amphetamine. Reduction of brain dopamine, but not norepinephrine, with 6-hydroxydopamine produced an acute depression of responding which eventually recovered to pretreatment levels. A low dose of alpha-methyltyrosine, which did not affect responding in control rats, significantly depressed responding in the rats with brain dopamine reduced. This treatment did not alter responding of rats with norepinephrine reduced by 6-hydroxydopamine. A dopamine beta-hydroxylase inhibitor, U-14,624, depleted norepinephrine an additional 70% yet failed to alter self-stimulation in any of the groups. In other experiments, the 6-hydroxydopamine treatment which reduced brain dopamine was found to block the facilitation of self-stimulation produced by d-amphetamine. This facilitation of lateral hypothalamic self-stimulation was not influenced by treatments which reduced brain norepinephrine. An experiment suggesting that dopamine is of importance to locus coeruleus self-stimulation is also described. Implications of these data indicating a role for dopamine in self-stimulation responding are discussed in relation to the "catecholamine hypothesis of self-stimulation." 35 references. (Author abstract)

000301 Costall, B.; Fortune, D. H.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, W. Yorks. BD7 1DP, England **Biphasic changes in motor behaviour following morphine injection into the nucleus accumbens.** British Journal of Pharmacology (Basingstoke). 57(3):423P, 1976.

The effect of morphine on motor behavior after bilateral injection into the nucleus accumbens of rats was investigated. The drug produces an initial period of catalepsy which develops within 7 minutes and persists for 220 minutes, followed by a period of hyperactivity and stereotyped biting which persists for a further 200 minutes. The catalepsy phase is inhibited in a dose dependent manner by nalorphine and cyproheptadine but not only piperoxan or atropine. Cataleptic doses of haloperidol enhance the morphine induced catalepsy. Nalorphine, aceperone and piperoxan reduce the intensity of the hyperactivity/biting phase in a dose dependent manner. Cyproheptadine and fluphenazine are effective only in doses causing motor depression in normal animals. Atropine and propranolol do not attenuate the hyperactivity. It is concluded that the integrity of the nucleus accumbens is important to the production of this biphasic response to morphine. Dopamine and 5-hydroxytryptamine function appear important for the production of catalepsy, but noradrenergic mechanism may be more important for the production of hyperactivity. 4 references.

000302 Cox, Tom; Lee, Janet. Stress Research Group, Department of Psychology, University of Nottingham, Nottingham NG7 2RD, England **Noise stress and the effects of viloxazine (Vivalan), a new antidepressant on open field activity in rats.** Pharmacology Biochemistry and Behavior. 4(6):729-730, 1976.

The effects of continuous and predictable discontinuous background white noise were investigated at three intensities (70, 80 and 90 dB) on the behavioral response of rats to a small dose of the antidepressant viloxazine hydrochloride (Vivalan). The results showed that increasing the level of noise produced changes in activity which were dependent on its mode of presentation (type). The drug appeared to enhance these changes. 10 references. (Author abstract modified)

000303 Crawley, J. N.; Contrera, J. F. Department of Zoology, University of Maryland, College Park, MD 20742 **Intraventricular 6-hydroxydopamine lowers isolation-induced fighting behavior in male mice.** Pharmacology, Biochemistry and Behavior. 4(4):381-384, 1976.

Male mice with high isolation induced fighting tendencies were administered 200micrograms of 6-hydroxydopamine (6-OHDA) or vehicle intraventricularly and tested for fighting tendency for up to 10 weeks until sacrifice, and assayed for brain norepinephrine (NE) levels. A strong correlation was found between NE depletion and reduced fighting tendency after 6-OHDA treatment. The depressed fighting by mice with less than 200ng NE/g persisted throughout a series of test fights, indicating no recovery in fighting behavior throughout the survival time. 35 references. (Author abstract)

000304 Crnic, Linda Smith. University of Illinois at Chicago Circle, Chicago, IL 60680 **The effects of chronic lithium chloride administration on complex schedule performance, activity, and water intake in the albino rat.** Physiological Psychology. 4(2):166-170, 1976.

Experiments designed to examine the behavioral effects of lithium in the rat are conducted in order to probe the functional significance of the finding that lithium therapy of manic depressives results in the reduction of inappropriate high rate (mania) behaviors without an accompanying depression of normal activities and intellectual functions. Rats were trained on a multiple schedule consisting of fixed ratio, fixed interval, and timeout extinction requirements, and were subjected to lithium chloride in doses of 1.5, 2.5, and 3.0meq/kg/day administered for 15 days at a time. The performance on the 5 days preceding the drug was compared to the performance on the last 5

days of lithium treatment. While there was a significant increase in water consumption in the 2 higher dose groups, there was little effect on the schedule performance of the 2.5meq/kg dose group and no effect upon the activity of any group. The 3.0meq/kg dose tended to result in prolongation of the postreinforcement pauses on the fixed ratio portions of the schedule and to truncate the fixed interval response curve. These results neither support nor contradict the hypothesis that lithium acts selectively on high rate behaviors or timing. A reduction in the variability of the experimental paradigm and the necessity of examining behavior during long-term dosages appear to be warranted for the elucidation of the mechanism of lithium action upon behavior, particularly its therapeutic action on mania. 17 references. (Author abstract modified)

000305 Cutler, Margaret G. Department of Biological Sciences, Glasgow College of Technology, Glasgow, Scotland **Changes in the social behaviour of laboratory mice during administration and on withdrawal from non-ataxic doses of ethyl alcohol.** Neuropharmacology (Oxford). 15(8):495-498, 1976.

The effects of administering ethyl alcohol for 3 weeks at a level of 8% in the drinking water were examined by ethological analysis of encounters between male mice. During administration, treated mice showed more social investigation and less nonsocial behavior than control partners. Of the individual postures significantly altered in frequency among treated mice, scanning increased whereas eating and the social postures of investigating, nosing, and attending were increased. One day after ceasing the administration of alcohol, mice from the treated group showed tremors and an increase of flagging when approached by an unfamilar mouse. Treated mice also showed periods of immobility and a reduction in the strenous activity of jumping on and off bars. They also displayed a persistence of some of the behavioral changes induced during administration of alcohol; eating and investigating continued to be increased in frequency, and the frequency of nonsocial behavior was still reduced. The significance of these findings is discussed. 13 references. (Author abstract)

000306 Dadkar, N. K.; Dohadwalla, A. N.; Bhattacharya, B. K. Department of Pharmacology, Research Centre, Hoechst Pharmaceuticals Limited, Bombay 400-080, India **Influence of pheniramine and chlorpheniramine on apomorphine induced compulsive gnawing in mice.** Psychopharmacology (Berlin). 48(1):7-10, 1976.

The influence of antihistamines on apomorphine induced gnawing behavior in mice was described and the action of antihistimines on the reciprocal balance between dopaminergic/cholinergic mechanisms was studied by using various pharmacological agents which are known to interfere with these systems. Gnawing compulsion was shown to result from pretreatment with pheniramine, chlorpheniramine and mepyramine, indicating an influence of the activity of the biogenic amines in the CNS. Experimental blocking of biosynthesis of biogenic amines or their receptors (with physostigmine, alpha-methyl-p-tyrosine, haloperidol or phenoxybenzamine) resulted in an antagonistic effect on the antihistamine potentiation of gnawing behavior. It is concluded that both pheniramine and chlorpheniramine potentiate apomorphine gnawing by upsetting the cholinergic and dopaminergic balance in favor of dopaminergic dominance. 26 references.

000307 Davenport, John W.; Hennies, Richard S.; Carey, John C.; Bishop, Steven B. Regional Primate Research Center, Univ. of Wisconsin Madison, Madison, WI 53706 **Behavioral depression: thyroid interactions with orepinephrine-depleting drugs.** Pharmacology Biochemistry and Behavior. 5(1):87-89, 1976.

The way triiodothyronine (T3) modified behavioral depressions resulting from drugs which selectively deplete norepinephrine (NE) by inhibition of dopamine-beta-hydroxylase (DBH), the enzyme which converts dopamine to NE, was studied in rats. Temporary suppression of rats' barpressing, activity, and feeding by the DBH inhibitor FLA-63 (bis (4-methyl-1-homopiperazinylthiocarbonyl) disulfide) was synergistically potentiated by T3 treatment. The increased severity and duration of behavioral depression from the combination of mildly depressing doses of FLA-63 and T3 was most marked 36 to 72 h after FLA-63 and closely resembled the depressive syndrome produced by higher doses of FLA-63 alone in time and specific features; these depressions were more likely due to toxicity than to depletion of brain NE. T3 did not potentiate behavioral depression induced by diethyldithiocarbamate. This pattern of findings suggested an interpretation of the T3/FLA-63 synergism in terms of increased FLA-63 toxicity in hyperthyroidism. 7 references. (Author abstract modified)

000308 Davies, J. K.; Wallace, P. Department of Pharmacology, Chelsea College, University of London, England **The effect of drugs on various parameters of mouse behaviour in a modified head-dipping test.** British Journal of Pharmacology (Basingstoke). 57(3):474P, 1976.

The limitations of the head dipping test developed by Boissier and Simon (1962, 1964) are discussed. A modification permitting the observation of additional behavioral parameters is presented. In contrast to the findings with the unmodified test by Bradley et al (1968) and by Nolan and Parkes (1973), amphetamine, chlordiazepoxide, diazepam and amylobarbitone were found not to increase dipping significantly. However, rearing and crossing were stimulated in a dose dependent manner by chlordiazepoxide and by diazepam, and to a lesser extent by amylobarbitone. Both parameters were inhibited by amphetamine and chlorpromazine, the latter drug in doses producing overt signs of sedation. It is suggested that by choice of suitable parameters of mouse behavior, the test modification presented may be useful in detecting and distinguishing the activities of several classes of CNS acting drugs. 4 references.

000309 Davis, Michael; Aghajanian, George K. Department of Psychiatry, Yale University School of Medicine, 34 Park Street, New Haven, CT 06508 **Effects of apomorphine and haloperidol on the acoustic startle response in rats.** Psychopharmacology (Berlin). 47(3):217-223, 1976.

The hypothesis that stimulation of dopamine (DA) receptors facilitates the acoustic startle reflex was examined by testing the effects of apomorphine and haloperidol on the acoustic startle response in rats. Apomorphine markedly facilitates startle amplitude for about 40 min. after injection and then depresses startle over the next 40 min. Both the early facilitory effect and the later inhibitory effect are directly related to the dose. Haloperidol alone has only a slight depressant effect on startle but preadministration of haloperidol completely blocks both the early facilitory effect and the later inhibitory effect of apomorphine. It is suggested that a previous investigator (Fechter, 1974) failed to find the augmentation of startle by apomorphine because startle was only measured 40 min. after injection. The hypothesis that DA receptor stimulation enhances acoustic startle amplitude is supported. 42 references. (Author abstract modified)

000310 Deikel, Stuart M.; Carder, Brooks. Univ. of California, Los Angeles, 405 Hildegard Ave., Los Angeles, CA 90024 **Attenuation of precipitated abstinence in methadone-dependent rats by delta9-tetrahydrocannabinol.** Psychopharmacology Communications. 2(1):61-62, 1976.

The attenuated symptoms of precipitated abstinence in methadone dependent rats by delta9-tetrahydrocannabinol is briefly reported through references in the literature. It is stated that naloxone precipitated symptoms are not necessarily specific to opiates and it has been suggested that treatment with nonnarcotic agents followed by naloxone will lead to the abstinence syndrome. 6 references.

000311 Delgado, J. M. R.; Grau, C.; Delgado-Garcia, J. M.; Rodero, J. M. National Center "Ramon y Cajal" and Autonomous University Medical School, Madrid, Spain **Effects of diazepam related to social hierarchy in rhesus monkeys.** Neuropharmacology (Oxford). 15(7):409-414, 1976.

The possibility that the pharmacological reactivity of experimental animals can be modified by changes in their hierarchial status was investigated. Rhesus monkeys were observed alone and when paired with a dominant partner or a submissive partner. Mobility was recorded by telemetry. Behavior was recorded every 5 seconds for eight 15 minute sessions. The effects of oral administration of 0.1mg/kg, 0.3mg/kg, 1.0mg/kg, 3.0mg/kg and 10mg/kg doses of diazepam were also observed. All tests were performed in the same environments so that the social situation was the only variable. In the control tests, mobility is independent of social situation, with similar mobility being observed in single animals, paired animals, dominant animals and submissive animals. Taking of food pellets delivered automatically every 30 seconds decreases significantly when the animals are paired rather than alone, with dominant animals taking significantly more food than submissive animals. Administration of 0.1mg/kg and 0.3mg/kg doses of diazepam do not produce changes in single or dominant animals, but significant effects occur on the behavioral profiles of submissive monkeys. Administration of 3.0mg/kg and 10mg/kg doses of diazepam produce diminution of body mobility in all situations, being more prominent in submissive monkeys. Food intake also diminishes. In dominant animals, no changes occur in locomotion, drinking, picking, or grooming. Administration of 0.1mg/kg of diazepam decreases aggressive acts by 50%. The natural order of dominance is not reversed even after administration of the highest dose. Admi nistration of diazepam to the submissive animal decreases aggressive behavior of the dominant animal, perhaps reflecting the diminished challenge to its authority. It is concluded that submissive animals show an extreme sensitivity to diazepam, and that individual hierarchy is an important element in the behavioral effects of the drug. This experimental procedure should be useful for future testing of psychopharmacological agents, especially those which could improve the social adaptability of mental patients. 25 references. (Author abstract modified)

000312 Deviche, P.; Balthazart, J. Laboratoire de Biochimie Generale et Comparee, Universite de Liege, 17, Place Delcour, B-4000 Liege, Belgium **Inhibition of adult social behaviour in ducks induced by juvenile administration of gonadal homones.** Behavioural Processes (Amsterdam). 1(1):41-56, 1976.

The long-term behavioral effects of gonadal hormone injections into domestic ducklings were studied. The inhibition of social displays is consistent with the view that these behavior patterns are regulated by the pituitary gonadal axis and the different levels at which the functional inhibition could have occurred are discussed. Far fewer social displays were performed by the males presented with injected females which showed less sexual behavior than the control females. It is concluded that the female plays an important part in the social display of ducks. 33 references. (Author abstract modified)

000313 Dobrzanski, S.; Doggett, N. S. Department of Applied Pharmacology, Welsh School of Pharmacy, King Edward VII Avenue, Cardiff, CG1 3NU England **The effects of (+)-amphetamine and fenfluramine on feeding in starved and satiated mice.** Psychopharmacology (Berlin). 48(3):283-286, 1976.

The effects of dextroamphetamine and fenfluramine were examined in: 1) mice adapted to eat only during a 3 hr period in the daytime (starved mice); 2) mice having free access to food, with food intake measured at night (free feeding mice); and 3) mice having free access to food, with food intake measured during the day (satiated mice). Dextroamphetamine and fenfluramine both produced a dose dependent depression of food intake in the starved mice, but only dextroamphetamine caused hyperactivity. Dextramphetamine and fenfluramine also produced a dose related depression of food intake in the free feeding mice but larger doses were required to produce a significant effect. Only dextroamphetamine caused hyperactivity. In the satiated mice, dextroamphetamine increased food intake and caused hyperactivity; fenfluramine had no effect on activity or on feeding. Caffeine also increased feeding and activity in satitated mice. It is suggested that behavioral arousal may be a factor in increasing food intake in satiated mice; however a specific effect by dextroamphetamine and caffeine on the feeding centers of the satiated mouse cannot be ruled out. 16 references.

000314 Dolphin, A. C.; Jenner, P.; Marsden, C. D. Institute of Psychiatry and King's College Hospital Medical School, Denmark Hill, London, S.E. 5, England **The relative importance of dopamine and noradrenaline receptor stimulation for the restoration of motor activity in reserpine or alpha-methyl-p-tyrosine pre-treated mice.** Pharmacology Biochemistry and Behavior. 4(6):661-670, 1976.

Two animal models of Parkinsonism are employed to investigate the role of noradrenaline in the motor effects of levodopa. Pretreatment with reserpine or alpha-methyl-p-tyrosine (AMPT) causes cerebral amine depletion and reduction of motor activity, which can be reversed by levodopa. The effect of inhibitors of noradrenaline (NA) synthesis and antagonists of NA and dopamine (DA) receptors on the action of levodopa are studied. For comparison, the effects of such treatments on apomorphine action are investigated. The results suggest that full restoration of motor activity in reserpine or AMPT pretreated animals requires stimulation of both DA and NA receptors. 40 references. (Author abstract modified)

000315 Downey, Danniel James. University of Arizona, Tucson, AZ **Behavior and addiction: experimental studies of morphine dependence. (Ph. D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-8671 HC$15.00 MF$8.50 56 p.

Effects of morphine administration on performance of a barpress response and on acquisition of light/dark discrimination were studied, with emphasis on addiction behavior and tolerance levels. Subjects were injected with morphine in increasing dosages on alternate days to a ceiling dosage and maintenance schedule, producing a titration of response rates to very low levels which were maintained throughout the ex-

periment. In response to drug treatment, reinforcements earned initially were depressed in all drug treated groups and later readjusted to predrug levels, while activity was stimulated by continued drug administration. In other experimental phases morphine dosages were continued at highest dosages achieved, and the ability of subjects to acquire the discrimination studied. Results show that response rates were depressed in drug treated groups, although drug treated subjects continued to earn high levels of reinforcements, although not as high as controls. Increasing group dosages produced both stimulated and depressed behaviors at various times, with no obvious relation to dosage. Results substantiate some habituation effects while demonstrating depression of discrimination performance. (Journal abstract modified)

000316 Drew, Roger; Priestly Brian G. Department of Human Physiology and Pharmacology, University of Adelaide, Adelaide, South Australia 5001 **Hexobarbital sleeping time and drug metabolism in rats with ligated bile ducts -- a lack of correlation.** Biochemical Pharmacology (Oxford). 25(14):1659-1663, 1976.

The correlation between hexobarbital sleeping time and drug metabolism during the early stages of bile duct ligation (BDL) induced cholestasis was studied in rats. The duration of hexobarbital sleeping time, 2-24 hours after BDL, is approximately twice that of sham operated controls. No significant decrease in the activity of microsomal aminopyrine demethylase, aniline hydroxylase, hexobarbital oxidase of the amount of cytochrome P-450 is detected during this period. A further prolongation of hexobarbital sleeping time is observed 48-72 hours after BDL, and this is accompanied by a significant impairment of drug metabolism in vitro. The effect of BDL on hexobarbital sleeping time is independent of the route of administration. Thiopental sleeping time is prolonged at 12 and 72 hours after BDL. Zoxazolamine paralysis time is prolonged at 72 hours after BDL, but not at 12 hours. Plasma protein binding of hexobarbital and thiopental is not altered by hyperbilirubinemia. It is suggested that changes in drug metabolism are not responsible for the prolongation of hexobarbital sleeping time during the early phase of cholestasis caused by BDL. It is concluded that hexobarbital sleeping time is not a reliable index of the activity of heaptic microsomal drug metabolizing enzymes after BDL. A change in brain sensitivity to hexobarbital may be as important as a change in its rate of metabolism as a factor in producing a change in the duration of pharmacological response. Since BDL changes the duration of response to thiopental without apparent alteration in brain sensitivity, altered drug distribu tion should also be considered as a factor in sleeping time experiments. 23 references. (Author abstract modified)

000317 Dyer, Robert S.; Weldon, Douglas A.; Thoumaian, Armen H. Department of Environmental Medicine, John Hopkins University, 615 N. Wolfe Street, Baltimore, MD 21205 **Task-specific effects of d-amphetamine and blindness on BALB/cj mice.** Physiological Psychology. 4(2):175-179, 1976.

Task specific effects of blindness on BALB/cj mice are examined to further elucidate the findings that blindness increases open field locomotor activity and produces marked increases in intertrial crossing during the terminal phases of shuttle avoidance learning. A second purpose is to characterize those tasks which most effectively separate amphetamine injected BALB/c mice from controls. Four groups of mice (normal/saline injected, enucleated/saline injected, normal/amphetamine injected, enucleated/amphetamine injected) were observed in shuttlebox shock avoidance trials, and number of avoidances, number of spontaneous crossings and mean response latency for each animal's daily 25 trials were recorded. Results indicated that optic enucleation increases activity in the photocell box and open field upon first exposure, but shuttlebox activity changes only occur after number of shocks/day decreases. Amphetamine did not affect open field, photocell box, or shuttlebox activity scores when shocks were absent. In the presence of shock, with or without learning contingencies, amphetamine did increase activity. 9 references.

000318 Eibergen, Robert Dennis. University of Pittsburgh, Pittsburgh, PA 15213 **Enhanced sensitivity to methamphetamine following chronic administration of methadone in the rhesus monkey and guinea pig: implications for extrapyramidal dyskinesias. (Ph.D dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-8801 HC$20.00 MF$10.00 246 p.

The influence of chronic administration of methadone on the pattern of behaviors elicited by methamphetamine in experimental animals was examined. In Experiment 1, rhesus monkeys consumed methadone for 291 to 650 days and were taken off the drug for 61 to 520 days. Small doses of methamphetamine elicited buccolingual dyskinesias in 7 of 8 former methadone Ss, but only in 1 of 11 controls. In Experiment 2, guinea-pigs were given twice daily injections of methadone or chlorpromazine for 35 days. Following termination of drug administration, methamphetamine elicited enhanced stereotyped behaviors in former methadone and chlorpromazine Ss, as compared with former saline controls. (Journal abstract modified)

000319 Elder, S. Thomas; McLean, Jack H. Department of Psychology, UNO-Lakefront, New Orleans, LA 70122 **Motor and visceral learning deficits in reserpine-treated rats.** Psychological Record. 26(2):233-241, 1976.

The effects of reserpine on the acquisition of motor and visceral learning behavior are investigated in 110, 210, and 310 day old rats. Subjects were trained to display immobility and defecation in a grid box while under the influence of 0, 0.5, 1.5, or 2.5mg/kg reserpine. Drug injections were given every 48 hours and began 7 days prior to training. Acquisition consisted of one training trial per day for 5 days, and was followed by 5 days of extinction at the rate of two trials per day. The results showed substantial dose dependent weight losses over all three age groups. Weight loss was found also to be a function of the training procedure, with the younger rats showing the greatest decrements. In addition, it was determined that reserpine treated animals experienced considerable difficulty learning a new motor and visceral response, thereby raising the possibility that reserpine treatment and instrumental blood pressure conditioning may be incompatible procedures for controlling essential hypertension. In addition, it was suggested that age of the adult subject be included more frequently as an independent variable in further behavioral and pharmacological studies. 20 references. (Author abstract modified)

000320 Estler, C.-J. Pharmakologisches Institut der Universitat, Krankenhausstr. 12, 852 Erlangen, West Germany /**Effect of methamphetamine on motor activity in young and old mice.**/ Der Einfluss von Methamphetamin auf die Laufzeit junger und alter Mause. Aktuelle Gerontologie (Stuttgart). 5(11):639-640, 1975.

In an investigation of the effect of methamphetamine on the running time of mice it was found that 3micrograms/g methamphetamine produced significantly less increase in

motor activity in older mice (20 months) than in young mice (4-6 weeks). The mice were kept at 25 degrees C room temperature and were given a standard feed (Herilan) ad libitum. Running activity was recorded by the method of Estler and Ammon. Further tests showed a decrease in body temperature because older mice apparently cannot make use of their substrate reserves as can younger mice. The lowered response of the central nervous system and the metabolic deficiencies both appear to be significant factors in the effects of methamphetamine. 3 references.

000321 Ezer, E.; Szporny, L. Chemical Works of Gedeon Richter Ltd. Pharmacological Laboratory, Budapest X, Hungary **Tape test as a simple new method for the study of compounds increasing the problem-solving ability of the rat.** Psychopharmacology (Berlin). 48(1):97-99, 1976.

A simple new method, the "tape test," is described for studying the enhancement of learning by drugs in "learning dull" rats. A piece of adhesive tape is pressed on the left front pad of the rats. The time of tape removal by the animal, i.e.,the problem-solving time, is measured. Rats unable to remove the tape within 60 sec observed on 3 consecutive days were selected as learning dull. The problem-solving ability of the rats was studied on 4 consecutive days, by posttrial administration. The problem-solving ability was found to be increased after treatment with different drugs such as para-chlorpehenylalanine (PCPA), pemolin, orotic acid, vitamin B12. The stimulatory effect of vitamin B12 could be inhibited by vincristine. 18 references. (Author abstract)

000322 Fehr, Kevin A.; Kalant, Harold; LeBlanc, A. Eugene. Department of Pharmacology, University of Toronto, Toronto, Ontario, Canada **Residual learning deficit after heavy exposure to cannabis or alcohol in rats.** Science. 192(4345):1249-1251, 1976.

Acute oral administration of cannabis extract to rats (tetraphydrocannabinol at 10mg/kg) impaired maze learning. The impairment was more marked after ten daily doses of the same size. After 1, 2, or 3 months' pretreatment with the same daily dose, followed by a 25 day drug free period, no residual learning impairment was found. However, 6 months of daily administration of cannabis (tetrahydrocannabinol, 20mg/kg) or alcohol (6/kg) produced significant residual impairment of learning of maze and motor coordination tasks, 2 months or more after the last drug administration. 15 references. (Author abstract)

000323 Ferri, S.; Santagostino, A.; Braga, P. C. Istituto di Farmacologia, 32, Via Vanvitelli, I-20129 Milano, Italy **Cross tolerance to antinociception elicited by intracerebroventricular administration of mescaline and morphine to rabbits, and EEG correlates.** Psychopharmacology (Berlin). 47(3):267-269, 1976.

Tolerance and cross-tolerance to the antinociceptive effects of equipotent doses of morphine and mescaline were studied by repeated intracerebroventricular administration in rabbits. Tolerance and cross-tolerance both occur. The recording of the electrical activity of different brain areas indicates that partial tolerance also develops to the EEG effects in animals undergoing chronic treatment with mescaline. The comparison of certain of the mescaline induced effects with those of morphine suggests that some biochemical and neural patterns are common to both drugs. 14 references. (Author abstract modified)

000324 Ferri, S.; Santagostino, A.; Braga, P. C. Istituto di Farmacologia, 32, Via Vanvitelli, I-20129 Milano, Italy **Development of tolerance to the antinociceptive effect of mescaline intraventricularly administered to rabbits.** Psychopharmacology (Berlin). 47(3):261-265, 1976.

Some effects of intraventricular injection of mescaline were examined in concious rabbits. Acute treatment with mescaline produces analgesia, the intensity of which is dose dependent. Daily administration of 100micrograms/Kg for 5 days produces complete tolerance to the antinociceptive effect. Tolerance also develops to the behavioral effects of mescaline with the exception of stupor, which is accentuated by chronic administration. An EEG arousal is induced by acute administration of mescaline; chronic administration produces a progressive slowing of the return of voltage to original levels. Comparison of certain of the mescaline induced effects with those of morphine suggests some biochemical and neural patterns common to both drugs. 14 references. (Author abstract modified)

000325 Flannelly, Kevin J.; Carty, Robert W.; Thor, Donald H. Edward R. Johnstone Training and Research Center, Bordentown, NJ 08505 **Vibrissal anesthesia and the suppression of intruder-elicited aggression in rats.** Psychological Record. 26(2):255-261, 1976.

The influence of perioral anesthesia upon the aggressiveness of established colony residents during encounters with unfamiliar male intruders is investigated. Male Long-Evans intruders (n=20) were individually exposed for 1 hr intervals to established colonies of Long-Evans rats consisting of three males and one female. Prior to introduction of the intruder, all colony males received either subcutaneous anesthetic injections (lidocaine HCL) or saline placebo injections into the vibrissal pads. Aggressive responding of the anesthetized male residents was significantly curtailed, but normal social interactions were undiminished. The results suggest that: (a) vibrissal sensation has a significant role in the maintenance of normal social aggression in the colony intruder paradigm, and (b) diminution of aggressive responding may not be attributed to a general decrease in all social behaviors. 17 references. (Author abstract modified)

000326 Flemenbaum, Abraham. Department of Psychiatry, Texas Tech University School of Medicine, Lubbock, TX **Lithium and amphetamine hyperactivity in rats: differential effect on d and l isomers?** Neuropsychobiology (Basel). 1(6):325-334, 1975.

Opposite pharmacological effects resulting from lithium and amphetamine were contended in order to explore the interaction between drugs at the animal level. Three groups, each one consisting of four rats, were put on chronic lithium condition to measure its effects on amphetamine hyperactivity. This condition was effected after appropriate handling and saline control periods and the baselines for drug activity were measured. In young rats lithium significantly decreased d-amphetamine hyperactivity (and probably other effects, like anorexia) while producing little effect on amphetamine stereotyped behavior (ASB). If confirmed, this fact may prove of marked importance in further localizing and studying the pharmacology of lithium. However, this observation was true in only three rats of the first group. All other rats, of the older group or of the other strain, showed only ASB, a fact that also deserves further study because it seems to contradict previous important reports. 31 references. (Author abstract modified)

000327 Ford, Robert D.; Balster, Robert L. Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Schedule-controlled behavior in the morphine-dependent rat.** Pharmacology Biochemistry and Behavior. 4(5):569-573, 1973.

The behavioral effects of acute and chronic administration of morphine and its withdrawal were studied using schedule controlled responding in the rat under a differential reinforcement of low rates of responding (DRL) schedule of food presentation. Acute morphine administration had a biphasic effect on response rate. Low doses (1.8-5.6mg/kg) tended to produce a small increase and higher doses (10-30mg/kg) decreased responding. Physical dependence was produced by twice daily injections, with an initial dose of 40mg/kg/day which was increased by 80mg/kg/day until reaching 600mg/kg/day which was continued for 14 days. Throughout chronic administration the pattern of responding remained disrupted resulting in a 27-47% decrease in presentations of the reinforcer, while response rate was more variable and generally decreased. The effects of morphine withdrawal lasted 5 days and produced an initial marked decrease in reinforcements per hour and biphasic change in response rate. A marked decrease in responding early in withdrawal (22.5hr) was followed by a marked and more prolonged (70.5-118.5hr) response rate increase. It is concluded that the behavioral sequelae to chronic morphine administration and morphine withdrawal can be studied conditions suitable for careful quantification. It is suggested that schedule controlled behavior may provide a useful means of evaluating drugs for physical dependence liability. 20 references. (Author abstract modified)

000328 Freed, William J.; Michaelis, Elias K. Dept. of Human Development, Univ. of Kansas, Lawrence, KS 66045 **Effects of intracisternal GABA or glutamic acid upon behavioral activity in the rat.** Pharmacology Biochemistry and Behavior. 5(1):11-14, 1976.

Rats were injected intracisternally with either saline or one micromole of gamma-aminobutyric acid (GABO) or its excitatory precursor, glutamic acid, and the behavioral activity of the rats in a novel environment was recorded as the rats habituated over the course of the subsequent 4 hours. The activity of the animals that were injected with GABA was greatly decreased, while the activity of the animals that were injected with glutamic acid was apparently unaffected, as compared to animals given saline. These data provide support for the hypothesis that GABA functions as an inhibitory neurotransmitter for behavior activating command neurons. 36 references. (Author abstract modified)

000329 Gaebelein, Claude J. Department of Psychiatry, Division of Health Affairs, Medical School, University of North Carolina, Chapel Hill, NC 27541 **/Heartrate learning after d-tubocurrarine administration in animals./** no title. Psychophysiology. 13(4):370, 1976.

A critique of a recent paper by Middaugh, Eissenberg and Brenner (Psychophysiology, 1975) is presented in a letter to the editor. The authors had concluded that animals maintained at a peak inspiratory pressure of 12cm of water after administration of d-tubocurarine chloride not only demonstrated evidence of instrumental heartrate learning but displayed heart rates comparable in frequency and variability to those of noncurarized animals. This finding may have been due to the method by which the d-tubocurarine chloride was administered which differed from the method of administration used in other studies reported in the same paper. It is suggested that the attribution of operant conditioning effects to a peak inspiratory pressure of 12cm of water is not warranted, and that the effect may have resulted from this manipulation, from the alteration in the method of drug administration, or both. 1 reference.

000330 Gauron, Eugene F.; Rowley, Vinton N. Department of Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IO 52242 **Chronic methylphenidate effects on learning in an F2 generation.** Journal of General Psychology. 95(first half):71-76, 1976.

Chronic methylphenidate effect on the learning of undrugged second generation rat offspring were investigated. The weaned offspring of 48 female albinos, previously treated with high or low drug doses or receiving placebo injections (controls), were tested on avoidance conditioning. Results indicated that: 1) learning of undrugged second offspring was affected; 2) differential sex effects occurred, with females making significantly more correct responses than males; and 3) some reproductive difficulties were encountered in second generation offspring. It is concluded that dosage and duration are not critical variables in modifying cross-generational behavior; and that regardless of drug utilization, these variables are not as relevant in chronic drug studies as in acute ones. Some indication of breeding disturbance in the F2 generation is noted. 4 references. (Author abstract modified)

000331 Gay, Patricia E.; Cole, Sherwood O.; Leaf, Russell C. Department of Psychology, Camden College of Arts and Sciences, Rutgers University, Camden, NJ 08102 **Interactions of amygdala lesions with effects of pilocarpine and d-amphetamine on mouse killing, feeding, and drinking in rats.** Journal of Comparative and Physiological Psychology. 90(7):630-642, 1976.

An investigation was carried out to determine whether the most effective method for inducing mouse killing in control rats could also induce mouse killing by amygdala lesioned rats, and whether amygdala lesions would attenuate the inhibitory effects of d-amphetamine on mouse killing. Repeated injections of 7.5mg/kg pilocarpine induced mouse killing in both amygdala lesioned and sham operated rats, but more injections were required in the lesioned animals. Killing was evoked least readily in rats that showed substantial weight loss after surgery and that had damage to more medial regions of the amygdala. d-Amphetamine, administered either before or after a killing test, inhibited pilocarpine induced killing in both surgical groups. Amygdala lesions attenuated pilocarpine facilitated drinking in sated animals, but did not alter the inhibitory effects of either pilocarpine or d-amphetamine on feeding or drinking. It is suggested that amygdaloid sites may play a role in the response facilitating effects of pilocarpine both on mouse killing and on drinking. It is also suggested that the amygdala is, at best, only a portion of a system mediating the inhibitory effects of d-amphetamine on killing, feeding, and drinking. 52 references. (Author abstract modified)

000332 Gianutsos, Gerald; Lal, Harbans. Department of Pharmacology, Michigan State University, E. Lansing, MI 48824 **Blockade of apomorphine-induced aggression by morphine or neuroleptics: differential alteration by antimuscarinics and naloxone.** Pharmacology Biochemistry and Behavior. 4(6):639-642, 1976.

The ability of neuroleptics and morphine to antagonize the action of a dopaminergic agonist, apomorphine, was investigated to examine their dopamine blocking action. Both morphine and the neuroleptics, haloperidol and oxyperomide, dose dependently reduce the aggression in rats produced by 20mg/kg of apomorphine, a dopamine receptor stimulant. The narcotic antagonist, naloxone, prevents the effect of morphine but not the effect of neuroleptics. Dexetimide, a centrally acting antimuscarinic drug, antagonizes the reduction in aggression produced by the neuroleptics, but does not affect the ac-

tion of morphine. The cholinergic agonist, pilocarpine, enhances the action of oxyperomide. These results suggest that a cholinergic component contributes to the antiagression action of neuroleptics and demonstrates a difference in the mechanism of action between neuroleptics and morphine. 21 references. (Author abstract)

000333 Gibbs, Marie E. Department of Psychology, LaTrobe University, Bundoora Victoria 3083, Australia **Modulation of cycloheximide-resistant memory by sympathomimetic agents.** Pharmacology Biochemistry and Behavior. 4(6):703-707, 1976.

The effect of amphetamine on memory and its relationship to postulated actions on transmitter release is examined. In day-old chickens with one trial passive avoidance learning, there is a short-term, labile memory existing for 90 min following training under the influence of cycloheximide CXM. (Amphetamine has been shown to keep the memory at precisely the level exhibited by the labile, CXM resistant memory trace at the time of injection.)Norepinephrine, methoxamine (an alpha adrenergic stimulant) and isoprenaline (a beta adrenergic stimulant) each mimic the amphetamine effect in CXM pretreated chickens. That the action of amphetamine due to its release of norepinephrine is supported by the finding that it is blocked by both alpha adrenergic (piperoxane) and beta adrenergic antagonists (propranolol). It is suggested that this labile memory trace depends on the functioning of a sodium pump. Norepinephrine may be modulating memory formation by an action on the sodium pump since in preliminary biochemical assays norepinephrine stimulated the sodium pump (Na^+/K^+ ATPase) activity in chicken forebrain total homogenate. 23 references. (Author abstract modified)

000334 Ginsburg, Benson E.; Sze, Paul Y. Behavioral Genetics Laboratory, Department of Biobehavioral Sciences, University of Connecticut, Storrs, CT 06268 **Pharmacogenetic studies of the serotonergic system in association with convulsive seizures in mice.** In: Bernard, B., Aminergic hypotheses of behavior: reality or cliche? Rockville, MD, National Institute on Drug Abuse, 1975. 149 p. (p. 85-95).

In a study of differences between strains of mice with regard to brain tryptophan hydroxylase (TPH) activity and its correlates, TPH activity was correlated with aggressive behavior and susceptibility to audiogenic seizures. Audiogenic seizure susceptibility in these strains and their hybrid F1's was inversely correlated with their brain TPH activities. Similarly, aggression scores in these genotypes were also inversely correlated with TPH activities. These results indicate that seizure susceptibility and aggression in mice may be related to the serotonergic activity in the brain. In the case of seizures, ethanol induced susceptibility to audiogenic seizures in mice was enhanced by reserpine, and the effect of reserpine could be reversed by 5-HTP but not by DOPA. Furthermore, p-chlorophenylalanine also enhanced such susceptibility, whereas alpha-methyltyrosine had no effect. In the withdrawal audiogenic seizures in mice during chronic ethanol treatment, adrenalectomy blocked the ethanol induced increase of brain TPH activity and also prevented the withdrawal seizures. These results are consistent with the hypothesis that the serotonergic system is among the components regulating excitability in the brain. 29 references.

000335 Goodall, Edwin B.; Vale, Hans E.; Carey, Robert J.; Lorens, Stanley A. Department of Pharmacology, University of Bergen, Bergen, Norway **Differential effects of morphine and amphetamine on medial frontal and lateral hypothalamic self-stimulation.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 196-198).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium in April 1975, results are given from a comparative study of the effects of morphine and amphetamine on electrical self-stimulation (SS) rate in the lateral hypothalamus (LH) and medial frontal cortex (MF). The study was performed to determine if the effects of the drugs are dependent upon the electrode locus. SS rates at both sites were differentially affected by the drugs. The SS rate in the MF was more resistant to the initial suppressive effects of morphine than that of the LH site, and the time course of development of peak SS rate facilitation following morphine injection differed at the two sites. While amphetamine isomers had qualitatively similar facilitative effects on SS rate at both electrode sites, only LH SS rate was significantly increased, and at this site the d isomer had a consistently greater peak facilitatory effect than the l isomer. This differential sensitivity of MF and LH SS behavior appeared mediated by different neuroanatomical and/or neurochemical systems and suggests that the phenomenon of SS cannot be interpreted on the basis of a unitary, positively reinforcing system in the brain. 8 references.

000336 Goodall, Edwin Baker, III. Syracuse University, Syracuse, NY **The effects of D- versus L-amphetamine, food deprivation, and current intensity on self-stimulation of the lateral hypothalamus, substantia nigra, and medial frontal cortex of the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-7650 HC$20.00 MF$10.00 94 p.

In order to evaluate the specificity of pharmacological and behavioral manipulations which have been demonstrated to alter intracranial self-stimulation response rate at medial forebrain bundle electrode sites, intracranial self-stimulation was studied in rats with chronically implanted lateral hypothalamic, substantia nigra, or medial frontal cortex bipolar electrodes. A comparison of the effects of d-amphetamine l-amphetamine on intracranial self-stimulation response rate indicated that the d-isomer was more potent than the l-isomer in facilitating lateral hypothalamic but not substantia nigra self-stimulation. Also, neither amphetamine isomer significantly affected medial frontal cortex self-stimulation. D-amphetamine resulted in a dose related increase in motor activity, while the same doses of the l-isomer resulted in decreased motor activity. Only lateral hypothalamic intracranial self-stimulation response rates increased significantly in response to food deprivation. Increases in current intensity above the level used for amphetamine and food deprivation testing facilitated lateral hypothalamic and substantia nigra self-stimulation rates, but did not significantly affect medial frontal cortex response rates. The responsiveness of intracranial self-stimulation at each electrode site is discussed in consideration of the correlation of each site with the fiber and cell body densities of catecholaminergic systems in the brain. (Journal abstract modified)

000337 Goudie, A. J.; Thornton, E. W.; Wheeler, T. J. Psychology Department, University of Liverpool, P.O. Box 147, Liverpool L69 3BX, England **Drug pretreatment effects in drug induced taste aversions: effects of dose and duration of pretreatment.** Pharmacology Biochemistry and Behavior. 4(5):629-633, 1976 .

The effects of chronic pretreatment with 3mg/kg daily doses of methamphetamine on the conditioned taste aversions produced by 3mg/kg methamphetamine, 10mg/kg

methamphetamine, 5mg/kg p-chloramphetamine, 5mg/kg fenfluramine and 20mg/kg morphine were studied in rats. The effectiveness of a 3mg/kg dose of methamphetamine in inducing a conditioned taste aversion to saccharin is reduced by chronic pretreatment with the same dose of the drug. The degree of attenuation of the aversion properties of methamphetamine is directly proportional to the duration of pretreatment ; nine or more daily injections completely abolish the aversive properties of the drug. Such a regime reduces only slightly the aversive properties of a 10mg/kg dose of methamphetamine and is ineffective in attenuating the aversive effects of the other drugs studied. It is suggested that attenuation of the aversive properties of a drug during chronic administration results from the development of tolerance to the drug. 15 references. (Author abstract modified)

000338 Gray, Peter; Solomon, Jolane; Dunphy, Marilyn; Carr, Frances; Hession, Michael. Department of Psychology, Boston College, Chestnut Hill, MA 02167 **Effects of lithium on open field behavior in "stressed" and "unstressed" rats.** Psychopharmacology (Berlin). 48(3):277-281, 1976.

An investigation was carried out to determine whether the effect of lithium on motor activity of rats varies as a function of environmental conditions of stress. Lithium chloride treated rats and saline treated controls were tested in an open-field apparatus illuminated by a moderate white light (stress condition) or dim red light (nonstress condition). In a second experiemtn, some rats received an electric foot shock (stress condition) and open field behavior was compared with that of rat receiving no shcok (nonstress condition). In both experiments, lithium significantly decreased rearing behavior in the rats in the stress conditions but did not affect performance by rats in the nonstress conditions. Lithium decreased horizontal locomotion in both stressed rats and unstressed rats. Lithium treated animals deficated less than saline treated rats during the first testing session but not in subsequent sessions. 16 references. (Author abstract modified)

000339 Gronan, Robert Joseph. University of Louisville, Louisville, KY **The influence of environmental novelty and time of day on the effects induced by 5-hydroxytryptophan in mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-16332 HC$15.00 MF$8.00 143 p.

Mice were allowed to habituate to the activity measuring apparatus before drug administration (L-alpha-hydrazino-alpha-methyldopa followed by the serotonin percursor 5-hydroxytryptophan, 5-HTP) and were then tested during the light/dark cycle to determine the influence of environmental novelty and time of day on the effects of 5-HTP. 5-Hydroxytryptamine increased locomotor activity at each of the periods investigated, but the locomotor depressive effect could generally be distinguished only during the dark periods, when control animals were most active. However, the stimulatory effect of 5-hydroxytryptamine on investigatory activity, a measure of rearings, sniffings, and biting of the sides of the testing cage, was also reduced or nonexistent during the light periods, as was the subsequent drug induced decrease in this measure. It was concluded that the biphasic activity effects of 5-HTP are due to a very large increase in 5-hydroxytryptamine turnover, associated with a slight decline in forebrain norepinephrine and dopamine during the period of hyperactivity, and substantial depletion of norepinephrine during the period of reduced activity. 5-HTP stimulation of investigatory activity is only demonstrated during the late light and early dark and middark periods, but this differential effect could not be associated with neurochemical differences. (Journal abstract modified)

000340 Herberg, L. J.; Franklin, K. B. J. Institute of Neurology, National Hospital for Nervous Diseases, Queen Square, London WC1N 3BG, England **The 'stimulant' action of tryptophan-monoamine oxidase inhibitor combinations: suppression of self-stimulation.** Neuropharmacology (Oxford). 15(6):349-351, 1976.

Induction of hyperactivity, including locomotor activity, in rats by injection of L-tryptophan (25mg/kg to 100mg/kg i.p.)after pretreatment with a monoamine oxidase inhibitor (pargyline, 75mg/kg) was confirmed. Hyperactivity was accompanied by tremor, vocalization and epileptiform manifestations, and occurred only after lethal or near lethal doses. Unlike catecholamine releasing stimulants such as amphetamine, monoamine oxidase inhibitor/L-tryptophan combinations did not facilitate self-stimulation performance, but suppressed it. Differences in the effects of monoamine oxidase inhibitor/L-trypotophan and amphetamine suggest differing central actions. Hyperactivity after monoamine oxidase inhibitor/L-tryptophan may represent a pre-ictal phenomenon and may not constitute an appropriate model for the reputed antidepressant action of monoamine oxidase inhibitor/L-tryptophan combinations in depressive illness. 16 references. (Author abstract)

000341 Hine, B.; Torrelio, M.; Gershon, S. no address **/Response to Deikel and Carder's article "Attenuation of precipitate abstinence in methadone-dependent rats by delta9-THC"./** Rejoinder by Hine, Torrelio, and Gershon. Psychopharmacology Communications. 2(1):63-65, 1976.

A rejoinder to Deibel and Carder's article, "Attenuation of Precipitate Abstinence in Methadone Dependent Rats by Delta9-THC," is presented by three cited authors claiming misrepresentation of their position. There is no conflict with the fact that isolated components or responses which comprise abstinence syndromes ordinarily resulting from narcotic dependence can be induced or modified separately under appropriate conditions of drug or environmental manipulation. The generality of the statement is questioned regarding whether treatment with nonopioids followed by naloxone will produce a true narcotic abstinence syndrome. It is stated that the original data supports the hypothesis that undesirable side-effects of THC treatment may be minimized by stabilization of addicts on methadone before detoxification. 3 references.

000342 Ho, I. K. 2500 North State St., University of Mississippi Medical Center, Jackson, MS 39216 **Systematic assessment of tolerance to pentobarbital by pellet implantation.** Journal of Pharmacology and Experimental Therapeutics. 197(3):479-487, 1976.

The development of tolerance to pentobarbital as measured by pentobarbital induced narcosis, hypothermia and toxicity was studied in mice. Rapid tolerance development to pentobarbital after pentobarbital pellet implantation is evidenced by a decrease in sleeping time after challenge with different doses of sodium pentobarbital ranging from 37.5-100mg/kg i.p. or a fixed dose of 75mg/kg i.p. of the drug. The sleeping time produced by sodium pentobarbital decreases by 50% after 1 day. After 2 or 3 days of implantation, the sleeping time is generally further decreased to 15-20% of the placebo control group. Tolerance to pentobarbital by pentobarbital pellet implantation also affects other pentobarbital induced responses such as hypothermia and lethality. In mice implanted with a 75mg pentobarbital pellet for 3 days, the degree and duration of pentobarbital induced hypothermia by intraperitoneal or in-

tracerebral administration of the drug is attenuated. Chronic administration of pentobarbital by 3 days of pellet implantation reduces the effect of sodium pentobarbital on lethality as evidenced by an increase in the LD50 of sodium pentobarbital after intraperitoneal or intracerebral administration of the drug. It is suggested that because pellet implantation of pentobarbital produces effects more slowly than does parenteral administration, the sequence of behavioral changes produced by pentobarbital can be more readily differentiated. This may permit study of the biochemical mechanisms involved in the initial effects of barbiturates which are essential for understanding the development of tolerance and physical dependence. 24 references. (Author abstract modified)

000343 Hollister, Alan S.; Breese, George R.; Kuhn, Cynthia Moreton; Cooper, Barrett R.; Schanberg, Saul M. 226 Biological Sciences Research Center, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC 27514 **An inhibitory role for brain serotonin-containing systems in the locomotor effects of d-amphetamine.** Journal of Pharmacology and Experimental Therapeutics. 198(1):12-22, 1976.

An inhibitory role for brain serotonin containing systems in the locomotor effects of d-amphetamine was hypothesized. Locomotor activity induced by d-amphetamine was found to be potentiated by food deprivation, a tryptophan free diet, p-chlorophenylalanine and drugs proposed to antagonize serotonin receptors in brain. Administration of L-tryptophan 1 hour prior to d-amphetamine injection was found to antagonize the enhanced response to d-amphetamine in starved rats and in rats which had tryptophan removed from their diet. However, tryptophan did not block the potentiated response to d-amphetamine in animals pretreated with p-chlorophenylalanine. These findings suggested that the antagonism of d-amphetamine induced activity by tryptophan in starved rats and rats fed a tryptophan free diet was not due to a nonspecific depressant effect of the amino acid. Since accumulation of d-amphetamine and its metabolites was not affected by any of the treatments which enhanced its activity, it seems unlikely that an alteration in the metabolism of d-amphetamine can explain these findings. The present work provides additional support for the view that serotonergic fibers play an important role in the actions of d-amphetamine. 50 references. (Author abstract modified)

000344 Holmgren, Bjorn; Urba-Holmgren, Ruth; Valdes, Mitchell. National Center of Scientific Investigation, Apartado 6990, La Habana, Cuba **Relative role of catecholamines in head-shaking of infant rats.** Pharmacology Biochemistry and Behavior. 5(1):29-34, 1976.

The relative contribution of catecholaminergic mechanisms in head shaking (H-S) of infant rats was explored by comparing the H-S inducing effects of apomorphine and amphetamine in rats from 4-4 days old, and the blocking effect of neuroleptic drugs (chlorpromazine and haloperidol) and more specific alpha-adrenergic and beta-adrenergic receptor antagonists (phenoxybenzamine and propranolol) on amphetamine induced H-S. As apomorphine, but not amphetamine, may induce H-S in 4-day-old rats, and the latter drug potentiates apomorphine induced H-S, even in days in which, if injected alone it has no effect, it is suggested that both dopaminergic and noradrenergic mechanisms are involved in H-S, thus differentiating this motor item from other motor patterns included in stereotyped behaviour. This suggestion is further supported by the demonstration that while D-amphetamine induced H-S is blocked by phenoxybenzamine, other stereotyped motor patterns continue unimpaired. 37 references. (Author abstract)

000345 Houser, Vincent P. RD No. 1, Box B95, Route 94, Chester, NY 10918 **The effects of chlorpromazine upon fear-motivated behavior in the squirrel monkey.** Physiological Psychology. 4(2):189-194, 1976.

The effects of chlorpromazine on behavior noted during aversive conditioned stimuli (CS) trials are investigated in order to obtain more evidence upon whether the Sidman nondiscriminated avoidance behavior schedule can detect the anxiolytic properties of the drug. Four male squirrel monkeys were subjected to an avoidance schedule (R-S, S-S -- 20 sec) that superimposed 3min CS/unavoidable shock pairings upon ongoing avoidance behavior. Three of the four animals demonstrated facilitated avoidance and activity rates during the CS, while one animal demonstrated suppressed avoidance and activity rates during the CS. Chlorpromazine (.05, .10, .20mg/kg) reduced overall response rates and augmented shock rates significantly in a dose related manner. The facilitation ratios computed to reflect the degree of response facilitation for three of the animals during the aversive CS were not significantly altered by drug administration. The one animal which normally suppressed its rate during the CS, however, demonstrated an attenuation of this suppression under all doses of the drug. These results were interpreted to suggest that the degree of behavioral facilitation noted during an aversive CS cannot be used as a sensitive index of the anxiolytic properties of drugs. 22 references. (Author abstract modified)

000346 Hunt, Glenn E.; Atrens, Dale M.; Chesher, Gregory B.; Becker, Frederick T. Department of Psychology, University of Sydney, Sydney 2006, N.S.W., Australia **Alpha-noradrenergic modulation of hypothalamic self-stimulation: studies employing clonidine, l-phenylephrine and alpha-methyl-p-tyrosine.** European Journal of Pharmacology (Amsterdam). 37(1):105-111, 1976.

An alpha-noradrenergic substrate of rewarding intracranial stimulation (ICS) has been hypothesized based on the observation that the alpha-antagonist phentolamine produced an inhibition of self-stimulation. The effects on hypothalamic self-stimulation of the alpha-agonist clonidine in normal and in catecholamine depleted rats was studied. Using a shuttlebox technique that provides a rate independent index of the rewarding and aversive components of ICS, it was demonstrated that clonidine produces a dose dependent inhibition of reward that is clearly dissociaable from any nonspecific effects of the drug. The ineffectiveness of the peripheral alpha-agonist l-phenylephrine indicates that the inhibition of reward produced by clonidine is mediated centrally. Clonidine and the catecholamine synthesis inhibitor alpha-methyl-p-tyrosine act together in a synergistic manner to greatly increase the magnitude and prolong the duration of the inhibition of reward while leaving the aversive component unaffected. These data are interpreted as supporting an alpha-noradrenergic basis of ICS reward while indicating that the aversive component of ICS is essentially independent of noradrenergic transmission. 21 references. (Author abstract modified)

000347 Irisawa, Naoki,; Iwahara, Shinkuro; Fukuda, Sachio. Department of Psychology, Tokyo University of Education, Tokyo, Japan **Abolition of the hippocampal theta activity and drug-learning dissociation.** Psychopharmacology (Berlin). 47(2):203-204, 1976.

Rats were trained to escape electric shock by running into one arm of a T-maze on 10 trial daily sessions with pentobarbital (10mg/kg), and to the opposite arm of the maze on other sessions with saline, the drug and saline sessions being alternated. This drug/learning dissociation or state dependent

learning was achieved by rats with medial septal lesions, abolishing hippocampal theta activity, as efficiently as rats with cortical lesions and intact rats. The suggested relationship between drug/learning dissociation and the suppression of hippocampal theta waves, produced by the drug, was not demonstrated. This finding provides further evidence that the usually assumed relationship between theta rhythms and behavior in normal rats does not always occur. In this connection, it may be noted that unpublished data showed increased fast activity induced by both pentobarbital and chlordiazepoxide, which was not altered by septal lesions. 6 references. (Author abstract modified)

000348 Ishikawa, Koichi; Saito, Shoji. Department of Pharmacology, School of Medicine, Nihon University, Tokyo 173, Japan **Differences in the effects of post-trial chlorpromazine, reserpine, and amphetamine on discrimination learning in rats.** Psychopharmacology (Berlin). 48(1):45-51, 1976.

The differences between the effects of chlorpromazine, reserpine and amphetamine on light/dark discrimination learning were demonstrated with posttrial injections in rats. Animals were trained to perform in discrimination learning reinforced by water for six days, then injected ip with the three centrally acting drugs after each training session. Differences in learning impairment of the three drugs administered immediately and 60 min after training were recorded. It was concluded that all three drugs impaired learning, but differed in their effects on learning; chlorpromazine impaired learning by a specific effect on learning itself; reserpine, by a nonspecific effect on behavior due to a long acting sedation; and amphetamine, by an effect to decrease the motivation to drink water. The specific effect of chlorpromazine can be related to the hypothesis of "memory trace" synthesis. 29 references. (Author abstract modified)

000349 Iwamoto, Edgar T.; Loh, Horace H.; Way, E. Leong. Department of Pharmacology, School of Medicine, University of California, San Francisco, CA 94143 **Circling behavior after narcotic drugs and during naloxone-precipitated abstinence in rats with unilateral nigral lesions.** Journal of Pharmacology and Experimental Therapeutics. 197(3):503-516, 1976.

The effects of acute narcotic drug administration and naloxone precipitated withdrawal were studied in rats with unilateral substantia nigra zona compacta (SNC) lesions. SNC in rats were produced by electrolytic coagulation or by an injection of 6-hydroxydopamine. Two to five weeks later, after being preselected for amphetamine induced ipsilateral circling behavior, the animals were administered narcotic agonists or narcotic antagonists and their circling behavior was observed. Morphine, methadone, levorphanol, nalorphine or pentazocine induced ipsilateral circling movements; naloxone and dextrorphan did not. Ipsilateral circling is also observed in rats with unilateral electrolytic lesions after administration of agents that are thought to enhance central dopaminergic activities: d-amphetamine, L-dopa and apomorphine. In rats with unilateral electrolytic or 6-hydroxydopamine SNC lesions that are rendered highly morphine dependent by multiple morphine pellet implantation, contralateral (C) circling behavior is observed within 1-2 mins after a naloxone challenge. The onset and duration of C circling behavior coincides with the initial appearance and duration of morphine withdrawal signs. C circling is also observed after administration of putative dopamine receptor blockers, haloperidol and pimozide, in rats with either unilateral electrolytic or 6-hydroxydopamine SNC lesions. Morphine pretreatment diminshes both the C circling intensity and the appearance of withdrawal signs observed after a naloxone challenge in morphine dependent, SNC lesioned rats. The naloxone precipitated withdrawal in unilaterally lesioned morphine dependent rats is accompanied by a 20% elevation of neostriatal dopamine in the intact side. In contrast to the effects of a chronic SNC lesion in decreasing neostriatal dopamine, a 77% increase in neostriatal dopamine is observed in the lesioned side 30 mins after electrolytic coagulation. It is suggested that narcotic agonists and partial agonists may enhance central dopaminergic activities and naloxone precipitated withdrawal may involve a diminution in central dipaminergic activities of the nigroneostriatal pathway. 64 references. (Author abstract modified)

000350 Iwamoto, Edgar T.; Loh, Horace H.; Way, E. Leong. Department of Pharmacology and Langley Porter Neuropsychiatric Institute, University of California, San Francisco, CA 94143 **Circling behavior in rats with 6-hydroxydopamine or electrolytic nigral lesions.** European Journal of Pharmacology (Amsterdam). 37(2):339-356, 1976.

Unilateral destruction of dopaminergic cell bodies in the substantia nigra zone compacta (SNC) was performed in rats by either electrocoagulation or chemical lesioning (6-hydroxydopamine, 6-OHDA), and the circling behavior of these rats was observed. The data confirm and extend previous studies and provide evidence that neuropharmacological differences do exist between electrolytic and 6-OHDA lesion circling behavior models, not only with respect to biochemical parameters, but also in their responses to drug induced circling behavior. When the two commonly employed lesion methods were compared, discrepancies between the two models were observed after administration of direct acting cholinergic and dopaminergic agonists. It is suggested that one circling behavior model be interpreted with caution and that comparable data from another model should be obtained and examined carefully. 36 references. (Author abstract modified)

000351 Iwasaki, Tsuneo; Ezawa, Kotaro; Iwahara, Shinkuro. Department of Psychology, Tokyo University of Education, 3-29-1 Otsuka, Tokyo, Japan 112 **Differential effects of chlordiazepoxide on simultaneous and successive brightness discrimination learning in rats.** Psychopharmacology (Berlin). 48(1):75-78, 1976.

Experiments were conducted to investigate the possibility that chlordiazepoxide (CDP) exerted differential inhibitory effects on simultaneous and successive discrimination learning. CDP at a dose of 20mg/kg ip was found to exert a marked disruptive effect on black/white successive discrimination learning in rats, while this effect failed to be obtained on black/gray simultaneous discrimination. Since trials to the learning criterion were found almost equal for saline rats on both successive and simultaneous discrimination tasks, the differential inhibitory effects of CDP could not be accounted for in terms of differences in difficulties of the two tasks. It is suggested that present results might be interpreted in terms of the hypotheses: 1) that CDP produces a deficit in the integration of relevant stimulus cues when they were presented across trials; or 2) that CDP has a disinhibitory effect in that inhibition of dominant response (positional preference) patterns is weakened by the drug, in a manner similar to effects observed in hippocampectomized animals. 14 references. (Author abstract modified)

000352 Jerussi, Thomas P.; Glick, Stanley D. Dept. of Pharmacology, Mount Sinai School of Medicine of the City Univ. of New York, 100th St. and 5th Ave., New York, NY 10029 **Drug-induced rotation in rats without lesions: behavioral and**

neurochemical indices of a normal asymmetry in nigro-striatal function. Psychopharmacology (Berlin). 47(3):249-260, 1976.

The effects of d-amphetamine, apomorphine, L-dopa, haloperidol and scopolamine on rotation (circling behavior) were studied in normal, nonlesioned rats. The rotation induced by amphetamine is significantly antagonized by alpha-methyl-para-tyrosine and by haloperidol but not by diethyldithiocarbamate. The rotation elicited by apomorphine is unaffected by alpha-methyl-para-tyrosine. High doses and low doses of amphetamine or amphetamine and apomorphine administered a week apart from each other do not necessarily induce rotation in the same direction. Dopaminergic/ cholinergic interactions were demonstrated; pilocarpine antagonizes amphetamine induced rotation but scopolamine does not. Scopolamine elicits rotation in the same direction as does amphetamine. Amphetamine is equally distributed to the two sides of the brain. Significant bilateral differences in striatal dopamine in rat brain are related to the direction of rotation. It is suggested that striatal dopamine is the neurochemical substrate for eliciting rotation in normal rats. It is also suggested that normal rats have asymmetrical levels of striatal dopamine as well as an asymmetrical complement of strital dopamine receptors. 60 references. (Author abstract modified)

000353 Johanson, Chris E.; Kandel, David A.; Bonese, Kathryn. University of Chicago, Pritzker School of Medicine, Department of Psychiatry, 950 E. 59th Street, Chicago, IL 60637 **The effects of perphenazine on self-administration behavior.** Pharmacology, Biochemistry and Behavior. 4(4):427-433, 1976.

Six rhesus monkeys prepared with intravenous catheters responded on a fixed-ratio 10 schedule for either an injection of cocaine or pentobarbital during a daily 3 hr session. The substitution of saline or various doses of perphenazine resulted in very low rates of responding. These results indicate that perphenazine, a piperazine substituted phenothiazine, is not a positive reinforcer. Pretreating animals maintained on cocaine with perphenazine resulted in increases in rate of self-administration at some doses and a decrease in rate at higher doses. The dose of perphenazine which resulted in the maximal increase in cocaine self-administration was directly related to the dose of cocaine maintaining responding. Pretreating animals maintained on of pentobarbital with perphenazine had no effect at doses which increased cocaine self-administration but decreased rate of pentobarbital self-administration at higher doses. These results indicate that perphenazine is capable of antagonizing some of the effects of cocaine. 21 references. (Author abstract modified)

000354 Jones, Elizabeth Anne Dozier. University of Tennessee, Knoxville, TN 37916 **Investigation of the interaction of d-amphetamine and amantadine hydrochloride using repeated acquisitions with serial reversal discrimination. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-11055, HC$15.00 MF$8.50 64 p.

Interaction of d-amphetamine and amantadine hydrochloride was studied employing serial discrimination reversals with repeated acquisitions, with emphasis on blockade of effects of d-amphetamine. Dose/response curves were determined independently for the drugs to optimize discrimination by d-amphetamine and disruption by amantadine hydrochloride. Analysis of the final experiment, in which amatadine hydrochloride was given as a pretreatment before d-amphetamine treatment, indicated that amantadine hydrochloride did not block effects of d-amphetamine on learning, but produced a synergistic effect rather than an inhibitory one. (Journal abstract modified)

000355 Joseph, J. A.; Appel, J. B. Behavioral Pharmacology Lab., Dept. of Psychology, Univ. of South Carolina, Columbia, SC 29208 **Alterations in the behavioral effects of LSD by motivational and neurohumoral variables.** Pharmacology Biochemistry and Behavior. 5(1):35-37, 1976.

Disruption of bar-pressing behavior was studied in rats that had been water deprived before they were given injections of the tryptophan hydroxylase inhibitor p-chlorophenylalanine methyl ester (PCPA) and later a low dose of lysergic acid diethylamide (LSD) in a study of the degree to which drug behavior interactions on underlying neuronal activity are determined by the degree of motivation (that is, the amount of deprivation of whatever reinforcer is maintaining its behavior). The rats were trained to bar-press on a fixed-ratio schedule of water reinforcement. They were then divided into two groups, one of which received 5 minutes of extra water 12 hours before each experimental session and the other which received no extra water. Half the animals in each group were then given three daily doses of PCPA while the remaining animals were given control injections of the PCPA vehicle. Ten days following the last administration of PCPA (or vehicle) all animals were given a low dose of LSD. Bar-pressing behavior was significantly disrupted only in those animals receiving both PCPA and extra water. Central (whole brain) concentrations of serotonin were significantly lower in all animals which had been treated with PCPA. These results suggest that amount of deprivation can be an important determinant of both the ability of drugs to alter behavior and the dependence of such alterations upon underlying neuronal activity. 12 references. (Author abstract modified)

000356 Kallman, M. D.; Isaac, W. Department of Psychology, University of Georgia, Athens, GA 30602 **Effects of amphetamine and illumination on activity following frontal ablation.** Physiology & Behavior. 16(5):641-643, 1976.

Hyperactivity in the rat resulting from the removal of the frontal lobe, including the head of the caudate putamen nucleus, in combination with d-amphetamine administration was studied in the light and dark over a 30 day postsurgical recovery period. Both d-amphetamine administration and frontal ablation increased activity level. In addition, d-amphetamine administration reversed the normal relationship of illumination with activity level. The postoperative hyperactivity following frontal ablation was dependent on the illumination level during testing. Potentiation of frontal induced hyperactivity by d-amphetamine was observed but the potentiation was not independent of the ambient illumination. 11 references. (Author abstract modified)

000357 Katz, R. J.; Thomas, E. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Effects of a novel anti-aggressive agent upon two types of brain stimulated emotional behavior.** Psychopharmacology (Berlin). 8(1):79-82, 1976.

The effects of antiaggressive agent Sch 12679 were evaluated upon stable baselines of rage and predation elicited by electrical stimulation of the hypothalamus in cats. Sch 12679 depressed approach and terminal aspects of both forms of attack. This is consistent with previous reports, and suggests the drug is effective in reducing many forms of aggression including brain stimulated emotional behavior. 13 references. (Author abstract)

000358 Keller, H. H.; Schaffner, R.; Haefely, W. Pharmaceutical Research Div., F. Hoffmann-La Roche & Co., Grenzacherstrasse 124, CH-4002 Basel, Switzerland **Interaction**

of benzodiazepines with neuroleptics at central dopamine neurons. Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(1):1-7, 1976.

The effect of benzodiazepines on the dopaminergic neurons originating in the mesencephalon in conditions of increased activity induced by neuroleptics is investigated. Several benzodiazepines markedly counteracted the elevation of the homovanillic acid (HVA) content of the rat brain induced by neuroleptics. A similar effect was obtained with the inhibitor of GABA transaminase, aminooxyacetic acid. The interaction of benzodiazepines with the neuroleptic induced HVA increase was similar in the striatum and in the limbic forebrain and was antagonized by the GABA receptor blocking agent picrotoxin. It is concluded that benzodiazepines, by intensifying GABA-ergic transmission, enhance the ongoing inhibition of mesencephalic dopamine neurons exerted by the striatonigral GABA system. A reduction of the neuroleptic induced increases of HVA and in the potentiation of the cataleptic effect of neuroleptics was also a result. 35 references. (Author abstract modified)

000359 Kelly, Paul T.; Luttges, Marvin W. Department of Aerospace Engineering Sciences, University of Colorado, Boulder, CO 80302 **Combined electroconvulsive shock and cycloheximide inhibition of brain protein synthesis in vivo.** Behavioral Biology. 17(2):219-224, 1976.

To determine if protein synthesis inhibition remains a viable candidate for explaining enhanced memory disturbances resulting from combined treatments with electroconvulsive shock (ECS) and cycloheximide (CXM), levels of mouse brain synthesis in vivo following such treatments were compared to levels following each treatment given separately. The duration of brain protein synthesis inhibition was examined for all treatment conditions. At appropriate times after treatment, mice were injected intracerebrally with labeled amino acids. The amount of radioactivity recovered from brain proteins after 5 minutes of labeling was used to estimate levels of synthesis. Although combined cycloheximide and electroconvulsive shock treatments have been shown to produce more complete behavioral amnesia than either treatment alone, such combined treatments do not produce more protein synthesis inhibition than cycloheximide alone. Hypotheses of memory storage based primarily on brain protein synthesis mechanisms may have to be reexamined. 14 references. (Author abstract modified0

000360 Keyes, D. M.; Janzik, H. H.; Mayer, K.; Eichner, M.; Gupta, D. Neurology Clinics of the University of Tubingen, Tubingen, West Germany **L-DOPA Effects on sexual behaviour: an experimental study.** Journal of Sex Research. 12(2):117-123, 1976.

Following the observation by Benkert (1972), that L-DOPA influences the sexual behavior of rats, the L-DOPA intraperitoneal induced sexual behavior in male Wistar rats, in relation to side-effects on blood hormone levels and via indirect side-effects of the sexual partner was studied. A percentage of time spent in sexual behavior was achieved by counting the number of sexual responses over a postinjection hour. A camera set to record 15 slides per minute was placed in the animal behavior room and thereby eliminated the necessity of distracting human observers. This film record also allowed a more slow and careful analysis by several different researchers at their own convenience. A record of individual animal behavior changes with time was also possible. L-DOPA brought about no definite change in amount of time spent in overall sexual activity, though it may have been responsible for an increase in the amount of time spent in mounting. Lowered luteinizing hormone levels would indicate that L-DOPA should cause a lowering of sexual responses due to lowered hormone level. This finding is contrary to almost all previous published data. Follicle stimulating hormone levels are elevated as expected, reflecting L-DOPA's hypothalamic stimulating effect. 14 references.

000361 Kokkinidis, Larry; Anisman, Hymie. Department of Psychology, Carleton University, Ottawa, Ontario, Canada K1S 5B6 **Interaction between cholinergic and catecholaminergic agents in a spontaneous alternation task.** Psychopharmacology (Berlin). 48(3):261-270, 1976.

The effects of various cholinergic drugs and catecholaminergic drugs on spontaneous alternation in a free running Y-maze task were studied in mice. Scopolamine reduced alternation to chance levels but dextroamphetamine in some doses produced alternation significantly below chance levels (perseveration). Physostigmine increased levels of alternation and reserpine was without effect. Reserpine effectively reversed the effects of scopolamine and physostigmine antagonized the perseveration induced by dextroamphetamine. When the animals were preexposed to the Y-maze the effects of amphetamine were enhanced but the effects of scopolamine were not modified. Scopolamine augmented the effects of amphetamine. It is suggested that: 1) cholinergic agents modify alternation by effects on habituation; 2) dextroamphetamine produces genuine perseveration without effectson habituation per se; and 3) alternation performance and perserveration are mediated by the interaction between the distinct behavioral effects of cholinergic activity and catecholaminergic activity. 34 references. (Author abstract modified)

000362 Kostowski, W.; Gajewska, Sylwia; Bidzinski, A.; Hauptman, Miroslawa. Dept. of Psychopharmacology, Psychoneurological Institute, Al. Sobieskiego 1/9, Warsaw, Poland **Papaverine, drug-induced stereotypy and catalepsy and biogenic amines in the brain of the rat.** Pharmacology Biochemistry and Behavior. 5(1):15-17, 1976.

The effects of papaverine on haloperidol induced catalepsy and apomorphine induced stereotypy as well as brain monoamines concentrations in rats were studied. Papaverine increased cataleptogenic effect of haloperidol reduced stereotypy induced by apomorphine. Slight but significant decrease in brain dopamine (DA) concentration was observed in rats treated with papaverine. The data provide the evidence that papaverine and haloperidol may act upon the same functional unit while apomorphine (being only poorly affected by papaverine) may attack different sites. The decreased DA concentration in brains of rats treated with papaverine is difficult to explain and further experiments including DA turnover and metabolite measurements are needed. 15 references. (Author abstract modified)

000363 Kovacic, Beverly; Domino, Edward F. Department of Pharmacology, Lafayette Clinic, 951 East Lafayette, Detroit, MI 48207 **Tolerance and limited cross-tolerance to the effects of N,N-dimethyltryptamine (DMT) and lysergic acid diethylamide-25 (LSD) on food-rewarded bar pressing in the rat.** Journal of Pharmacology and Experimental Therapeutics. 197(3):495-502, 1976.

The development of tolerance to the effects of N,N-dimethyltryptamine (DMT) and to lysergic acid diethylamide-25 (LSD) and the development of cross-tolerance between DMT and LSD was studied in the rat. Both LSD and DMT abolish food rewarded fixed ratio bar-pressing in a dose re-

lated fashion. Intraperitoneal injections of 3.2mg/kg DMT or 10mg/kg DMT every 2 hrs results in a worsening in daily bar-pressing during the first week of chronic treatment. After 6 days, rats receiving 10mg/kg DMT do not bar press at all. As the chronic injections continue, rates of bar-pressing gradually increase until responding is not disrupted at all by an injection of DMT. Rats receiving 3.2mg/kg DMT show cross-tolerance to an injection of 0.1mg/kg LSD. Another group of rats receiving injections of LSD (0.1mg/kg i.p.), once daily for 21 days and then three times daily for 4 days, became partially tolerant to the disruptive effects of LSD on bar-pressing. Cross-tolerance to a challenge injection of 10mg/kg of DMT does not occur. After an additional 3-5 days of LSD injections, complete tolerance to the effects of LSD occurs and the rats are also tolerant to 3.2mg/kg of DMT. It is suggested that disruption of bar-pressing is not mediated through interference with appetite and involves mechanisms different from or in addition to those producing the motor effects. It is further suggested that, at the doses used, LSD and DMT act via a common mechanism or on a final common pathway, and that DMT additionally acts on another mechanism which is unaffected by LSD. 17 references. (Author abstract modified)

000364 Kovacs, Gabor L.; Telegdy, Gyula; Lissak, Kalman. Department of Physiology, University Medical School, Pecs, Hungary **5-Hydroxytryptamine and the mediation of pituitary-adrenocortical hormones in the extinction of active avoidance behaviour.** Psychoneuroendocrinology (Oxford). 1(3):219-230, 1976.

Adult male albino rats were stimulated with light periodically, after being dosed with corticosterone, and correlated with hypothalamic and mesencephalic serotonin 5-hydroxytryptamine (5-HT) content, in order to study avoidance behavior. Active avoidance behavior was seen to be dose related in regard to corticosterone treatment. Adrenocorticotrophic hormone (ACTH) in doses of 2.0and 4.0i.m. per animal resulted in an increased hypothalamic and mesencephalic 5-HT content in intact animals, but there were no changes in cerebral 5-HT levels in adrenalectomized rats. Nialamide treatment (125 mg/kg), which increased brain 5-HT content, counteracted the effect of 10.0mg/kg corticosterone on extinction. Experimental results suggest that the action of corticosterone on active avoidance behavior is mediated, partly, by changed 5-HT metabolism in the brain. 40 references. (Author abstract modified)

000365 Kurtz, Perry James. Syracuse University, Syracuse, NY 13210 **Effects of reserpine on acquisition and retention of discriminated escape training. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-7660 HC$20.00 MF$10.00 148 p.

A discriminated escape training paradigm was used to study the effects of reserpine on learning and memory in mice. In the first experiment, intraperitoneal injection of reserpine 2 hours before reversal training had no effect on acquisition but did produce a dose dependent impairment of retention test performance 10 days later. The second experiment indicated that the degree of this retention impairment depended on the time interval between drug administration and reversal training. The possibility that reserpine may produce state dependent learning was explored in the third experiment. Retention impairments observed when a reserpine injection was given 2 hours before reversal training were not attenuated by readministering the drug before testing. In the last experiment it was found that when the catecholamine precursor l-dihydroxyphenylalanine and the indole amine precursor dl-hydroxytryptophan were both given after reserpine treatment, subsequent retention performance was not significantly impaired. (Journal abstract modified)

000366 Leander, J. David. Department of Pharmacology, School of Medicine, Swing Building, University of North Carolina, Chapel Hill, NC 27514 **Effects of d-amphetamine, pentobarbital, chlorpromazine and promazine on electric shock postponement responding by the pigeon.** Journal of Pharmacology and Experimental Therapeutics. 198(1):4-11, 1976.

The effects of d-amphetamine, pentobarbital, chlorpromazine and promazine on responding under schedules of electric shock postponement were studied in pigeons. Responding was maintained by three different response/shock intervals. Low doses of d-amphetamine increased response rates without decreasing shock rates under all three response/shock intervals and decreased the high response rate under the 10 second response/shock interval but did not decrease the lower rates of responding under the 20 sec and 60 sec response/shock intervals. Pentobarbital decreased the high rate of responding maintained under the 10 second response/shock interval at a lower dose than the lower rates of responding under the 20 sec and 60 sec response/shock intervals. The high dose of pentobarbital decreased responding and the low doses had no effect under all three response/shock intervals. Chlropromazine did not affect the average rate of responding under all response-shock intervals and only slightly increased shock rates under the 20 and 60 second response/shock intervals. Promazine increased the rates of responding and decreased shock rates under all three response/shock intervals. Analysis of the temporal patterns of responding within the response/shock interval showed that d-amphetamine tended to induce the animals to respond earlier than they normally would in the response/shock interval while otherwise maintaining the temporal pattern of responding, pentobarbital decreased the probability of responses late in the response/shock interval, and chlorpromazine increased the probability of responses in the middle of the response/shock interval, producing a lessening of the temporal patterning of responding within the response/shock interval. It is concluded that effects of pentobarbital and d-amphetamine are similar on responding under schedules of shock postponement across several species, whereas there are prominent species differences in effects of the phenothiazines, chlorpromazine, and promazine. 38 references. (Author abstract modified)

000367 Livingston, A.; Waterman, A. E. Department of Pharmacology, University of Bristol, University Walk, Bristol BS9 1TD, England **Effects of repeated doses of ketamine on sleeping times in rats.** British Journal of Pharmacology (Basingstoke). 57(3):457 p, 1976.

Ketamine (75mg/kg ip) was injected into rats every fourth day for 16 days in order to determine whether tolerance, exhibited as a decrease in sleeping time, occurs. Sleeping time was measured as the time elapsed between the loss and regaining of the righting reflex. Mixed venous and arterial blood samples were obtained at the point of recovery and assayed for ketamine, its N-demethylated metabolite, and its cyclohexanone oxidation product. In contrast to the findings of Douglas and Dagirmanjian (1975), no significant decrease in mean sleeping times occurred after repeated doses although a tendency toward decrease was noted at day 16. Plasma levels of ketamine decreased significantly by day 12; this decrease was balanced by a significant rise in plasma levels of the cyclohexanone oxidation metabolite. The presence of metabolite II directly contrasts with the findings of other investigators

(Cohen, Chan, Way, and Trevor, 1973; Cohen and Trevor, 1974 who found no evidence of this metabolite either in vivo or in vitro in rats. It is suggested that the induction of the enzyme responsible for the appearance of the cyclohexanone oxidation product may have occurred. 4 references.

000368 Lowe, Warren C.; O'Boyle, Michael. University of Southern Mississippi, Hattiesburg, MS 39401 **Suppression of cricket killing and eating in laboratory mice following lithium chloride injections.** Physiology & Behavior. 17(3):427-430, 1976.

The killing response and eating response of mice injected with lithium chloride after attacking crickets or after attacking and eating crickets were studied. Before lithium chloride treatment, most male Harlan/ICI mice killed crickets whether food deprived or not, indicating that the mouse/cricket model may serve as a convenient example of predation. Injections of lithium after attack or after eating were equally effective in suppressing cricket killing. Injections given after eating suppressed eating responses more than attack responses. It is suggested that different classes of aversive stimuli may be differentially effective in modifying predatory behaviors. 17 references. (Author abstract modified)

000369 Luttge, William G. Department of Neuroscience, University of Florida College of Medicine, Gainesville, FL 32610 **Intracerebral implantation of the anti-estrogen CN-69, 725-27: effects on female sexual behavior in rats.** Pharmacology Biochemistry and Behavior. 4(6):685-688, 1976.

Ovariectomized adult female rats were stereotaxically implanted with double walled cannulas and tested for sexual receptivity (lordosis behavior) following SC estradiol benzoate and progesterone priming. Implantation of the antiestrogen CN-69,725-27 immediately after the first of 3 daily estrogen injections produced a dramatic inhibition of sexual receptivity when these implants were placed in the preoptic and anterior hypothalanic areas. CN-69,725-27 implants had no effect on receptivity when implanted in the middle hypothalamus, mesencephalon or frontal cortex. All inhibitory effects of the antiestrogen were reversible within 1 day after removal of the CN-69,725-27 cannula from the brain. 25 references. (Author abstract)

000370 Majchrowicz, Edward; Hunt, Walter A. National Institute on Alcohol Abuse and Alcoholism, WAW Bldg., 2700 M. L. King Jr. Ave., S.E., Washington, DC 20032 **Temporal relationship of the induction of tolerance and physical dependence after continuous intoxication with maximum tolerable doses of ethanol in rats.** Psychopharmacology (Berlin). 50(2):107-112, 1976.

The relative rates of the development of tolerance and physical dependence after 1 day to 7 days of administration of maximum tolerable doses of alcohol were studied in rats. A significant degree of tolerance for all signs of intoxication (coma, loss of righting reflex, various degrees of ataxia, sedation and neutrality) occurred after 4 days of treatment but did not reach maximum level even after 7 days of treatment. The severity of the withdrawal symptoms (hyperactivity, tremors, spastic rigidity and spontaneous convulsive seizures) increased progressively when the drug was discontinued after 1 day to 4 days of treatment; continuation of treatment for longer periods of time did not produce a consistent accentuation of the withdrawal reactions. It is suggested that tolerance and physical dependence are mediated through different mechanisms. 45 references. (Author abstract modified)

000371 Malick, Jeffrey B.; Barnett, Allen. Biological Research Dept., ICI United States Inc., Wilmington, DE 19897 **The role of serotonergic pathways in isolation-induced aggression in mice.** Pharmacology Biochemistry and Behavior. 5(1):55-61, 1976.

Male mice that became aggressive following four weeks of social isolation were treated with seven known serotonin receptor antagonists. All of the antiserotonergic drugs selectively antagonized the fighting behavior of the isolated mice; the antiaggressive activity was selective since, at antifighting doses, none of the drugs either significantly altered spontaneous motor activity or impaired inclined screen performance. Antagonism of 5-hydroxtryptophan induced head twitch was used as an in vivo measure of antiserotonergic activity and a statistically significant correlation existed between potency as an antiserotonergic and potency as an antiaggressive. Parachlorophenylalanine, a serotonin depletor, also significantly antagonized isolation induced aggression for at least 24 h postdrug administration. The interrelationship between cholinergic and serotonergic mechanisms in the mediation of isolation aggression was investigated. The involvement of serotonergic systems in isolation induced aggression is discussed. 45 references. (Author abstract)

000372 Marcus, Richard; Carnathan, Gilbert; Meyer, Roger E.; Cochin, Joseph. National Institute on Drug Abuse, Rockville, MD **Morphine-based secondary reinforcement: effects of different doses of naloxone.** Psychopharmacology (Berlin). 48(3):247-250, 1976.

The effects of different doses of naloxone on morphine based secondary reinforcement were studied in rats. In the first day a neutral stimulus (buzzer) was repeatedly paired with intravenous morphine infusions. The next day the ability of the buzzer and saline infusion to support lever pressing was tested. High doses of naloxone blocked, and low doses of naloxone partially blocked this morphine based secondary reinforcement. Subjects in the medium naloxone group demonstrated an apparent avoidance of the lever, suggesting that the morphine infusions were aversive at this dosage level of naloxone. The secondary reinforcement tests reliably predicted behavior on a subsequent test for acquisition of morphine seeking behavior. 8 references. (Author abstract modified)

000373 Marshall, John F.; Friedman, Mark I.; Heffner, Thomas G. Psychobiology Program, Departments of Psychology and Psychiatry, University of Pittsburgh, Pittsburgh, PA 15260 **Reduced anorexic and locomotor-stimulant action of D-amphetamine in alloxan-diabetic rats.** Brain Research (Amsterdam). 3(2):428-432, 1976.

The behavioral effects of dextroamphetamine in rats made diabetic by injection of alloxan were investigated. Doses of amphetamine which produce a substantial decrease in food intake by control animals cause only a minor reduction in feeding in alloxan treated diabetic animals. In alloxan treated rats receiving insulin, amphetamine produces anorexia nearly as great as in the control animals. Amphetamine induced hyperactivity in alloxan treated diabetic rats is also much less than the hyperactivity produced in control animals. Although the accumulation of radiolabeled amphetamine in the brain and plasma of diabetic animals is slightly less than in control animals, it is suggested that the slight decrease cannot explain the attenuated behavioral effects of the drug. While the possibility exists that diabetes causes less amphetamine to reach the specific sites responsible for its behavioral effects, it is suggested that the altered response to amphetamine in diabetic rats is dependent upon the absence of insulin. 7 references.

000374 McCarty, Richard C.; Whitesides, George H. Department of Pathobiology, School of Hygiene and Public Health, Johns Hopkins University, 615 North Wolfe Street, Baltimore, MD 21205 **Effects of d- and l-amphetamine on the predatory behavior of southern grasshopper mice, Onychomys torridus.** Aggressive Behavior. 2(2):99-105, 1976.

Adult male and female southern grasshopper mice (Onychomys torridus) were tested for predatory aggression toward cricket prey 1 hr after single injections of d-amphetamine (1 or 10mg/kg) or l-amphetamine (1 or 10mg/kg). At the lower dose, d-amphetamine decreased feeding behaviors, while l-amphetamine altered attack related behaviors. At the higher dose, both stereoisomers appeared to be equipotent in significantly decreasing five measures of predatory aggression. These results suggest that brain dopamine and norepinephrine play important roles in the regulation of predatory aggression of Onychomys torridus. 28 references. (Author abstract modified)

000375 McGuire, Patricia Susan. University of Minnesota, Minneapolis, MN 55455 **The effect of acute methadone on fixed-interval schedules of reinforcement in pigeons. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-14996 HC$15.00 MF$8.00 108 p.

The effect of methodone on fixed-interval (FI) keypecking performance in pigeons was examined under three food reinforcement schedules. In the first experiment, a three component multiple FI schedule was used to analyze the effects of methadone on keypecking maintained by conditioned reinforcement. The second experiment examined in greater detail the effects of methadone on the keypecking performance of pigeons on a tandem fixed ratio, FR-3, (FI 30 second) schedule of food reinforcement. The third experiment compared the effects of methadone on performance on tandem schedules with performance on a FI schedule of the same value. The results of these three experiments suggest that performance on second order schedules of conditioned reinforcement is well maintained when injections of methadone are tested. This is not the case with schedules lacking conditioned reinforcers (tandem schedules) or schedules with only weak conditioned reinforcers (extended chain schedules). These findings suggest conditioned reinforcers may have an important function in maintaining behavior when methadone is administered. (Journal abstract modified)

000376 McLean, Jack H.; Kostrzewa, Richard M.; May, James G. Department of Psychology, University of New Orleans, New Orleans, LA 70122 **Behavioral and biochemical effects of neonatal treatment of rats with 6-hydroxydopa.** Pharmacology Biochemistry and Behavior. 4(5):601-607, 1976.

The effects of 6-hydroxydopa (6-OHDOPA) on the developing nervous system were investigated in rats. The agent was adminstered systemically on the 1st, 3rd, and 5th day of life. Behavioral testing was performed when the rats reached adulthood and was designed to assess 6-OHDOPA effects on a number of motivational variables, both appetitive and aversive, including food and water intake , copulation, approach/avoidance behavior in a straight runway, open-field activity, pain elicited aggression, and thermoregulation. Animals were sacrificed at 8 months or 12 months for brain catecholamine analysis. The treated rats exhibit impaired passive avoidance, less shock induced aggression and more locomotor open-field activity than saline controls. Male copulatory behavior, food and water intake, and thermoregulation are not affected. In comparison to saline controls, 6-OHDOPA treated rats contain elevated levels of endogenous norepinphrine (NE) in lower brainstem regions (e.g. midbrain and pons medulla) as well as in cerebellum. Hypothalamic NE levels is not affected. Significant depletions of NE in the hippocampus and neocortex suggest that the neurotoxic actions of 6-OHDOPA occur primarily in terminal regions of the dorsal noradrenergic bundle (DNB). Alterations in behavior may be attributed to central NE depletion, as no peripheral effects are observed at the age of testing and dopamine level is not affected. 47 references. (Author abstract modified)

000377 McLendon, David M.; Harris, Robert T.; Maule, William F. Department of Physiology, Baylor College of Medicine, 1200 Moursund Avenue, Houston, TX 77030 **Suppression of the cardiac conditioned response by delta-9-tetrahydrocannabinol: a comparison with other drugs.** Psychopharmacology (Berlin). 50(2):159-163, 1976.

The effects of delta-9-tetrahydrocannabinol (THC) on a physiological measure of anxiety, the cardiac conditioned response (CCR), were examined and compared with those of diazepam, chlorpromazine and morphine. THC blocks the CCR in a dose related manner. The effects of THC were similar to those of diazepam. Chlorpromazine and morphine affected the CCR in an unreliable manner; both drugs attenuated the response in some cases and potentiated it in other instances. It is concluded that THC, like diazepam, has a tendency to reduce anxiety as measured by the CCR. 17 references. (Author abstract modified)

000378 Melchior, Christine L.; Myers, R. D. Lab. of Neuropsychology, Purdue Univ., West Lafayette, IN 47907 **Genetic differences in ethanol drinking of the rat following injection of 6-OHDA, 5,6-DHT or 5,7-DHT into the cerebral ventricles.** Pharmacology Biochemistry and Behavior. 5(1):63-72, 1976.

The preference characteristics for ethanol of four different strains of rats were determined in a two way choice situation by offering water and ethanol in a concentration which was increased from 3% to 30% over a 12 day test sequence, and then 5,6-dihydroxytryptamine (5,6-DHT), 6-hydroxydopamine (6-OHDA) or 5,7-dihydroxytryptamine (5,7-DHT) were then injected acutely into the lateral cerebral ventrical in a study of genetic differences in ethanol drinking following injection. Rats of the Sprague-Dawley strain increased their ethanol preference following the lesioning of the serotonergic system by 5,6-DHT, whereas similar destruction of catecholaminergic neurons by 6-OHDA markedly suppressed ethanol intake; Long-Evans rats displayed a similar trend in ethanol drinking patterns. However, animals of the Holtzman strain manifested the increased drinking after 5,6-DHT, but showed no suppression of drinking following 6-OHDA. The preference of rats of the Wistar strain was unaffected by 5,6-DHT but attenuated by 6-OHDA. 5,7-DHT had little or no effect on ethanol consumption in any of these strains. These findings thus suggest that genetic factors are an important determinant in an animal's response to a drug that affects serotonim or norepinephrine systems in the brain, particularly when ethanol selection is investigated. 36 references. (Author abstract modified)

000379 Meyer, R. E.; Marcus, R.; Carnathan, G.; Cochin, J. McLean Hospital, Drug Addiction Research-H, 115 Mill Street, Belmont, MA 02178 **Narcotic blockade, length of addiction and persistence of etonitazene consumption in rats.** Psychopharmacology (Berlin). 47(3):273-279, 1976.

The effects of naloxone on relapse tendencies in previously addicted animals were investigated. It is suggested that stimuli

associated with the reinforcing properties of the opioid solution become strong conditioned reinforcers, capable of maintaining responding for long periods of time despite blockade of the reinforcement properties of the drug. 8 references. (Author abstract modified)

000380 Michenfelder, John D.; Milde, James H.; Sundt, Thoralf M., Jr. Department of Anesthesiology, Mayo Clinic, Rochester, MN **Cerebral protection by barbiturate anesthesia: use after middle cerebral artery occlusion in Java monkeys.** Archives of Neurology. 33(5):345-350, 1976.

The cerebral protective effect of barbiturate anesthesia in regional cerebral ischemia was examined in Java monkeys. Thirty min after middle cerebral artery occlusion, nine monkeys received pentobarbital sodium anesthesia which was maintained for 48 hr. Nine other animals received supportive care only. Seven of the control monkeys developed a cerebral infarction, three did not survive past the intitial 48 hr, and the other four had a notable neurologic deficit. All of the pentobarbital treated animals survived the observation period; four had a cerebral infarction and two of these had a notable neurologic deficit. In the other five monkeys, no infarct or notable deficit occurred. The clinical application of using barbiturate anesthesia to treat stroke in humans is discussed. 25 references. (Author abstract modified)

000381 Middaugh, Susan J.; Eissenberg, Ethel; Brener, Jasper. no address. **no title.** Psychophysiology. 13(4):370-371, 1976.

This letter is a reply to a critique by Claude J. Gaebelein of one of the authors' published studies (Psychophysiology, 1976). It is stated that in adequately ventilated rats, the levels of curarization commonly employed have little demonstrable cardiovascular effect. Although it is possible that depth of skeletal paralysis differs with the dose and method of administration used in the original study, it is concluded that, in the rat, with the levels of curarization and the methods of ventilation employed, d-tubocurarine chloride exerts little cardiovascular effect relative to respiratory factors, which are quite critical. 6 references.

000382 Miliaressis, Eleftherios; Jacobowitz, David M. Laboratory of Neurophysiology, University of Quebec, Chicoutimi, Canada **Hyperthemia following self-stimulation of the median raphe in the rat.** Pharmacology, Biochemistry and Behavior. 4(4):477-479, 1976.

The involuement of common nervous areas in self-stimulation and hyperthemia elicited by stimulation of raphe nuclei was investigated. Bipolar electrodes (200mu m in dia) were implanted stereotaxically in 31 male Sprague-Dawley rats (280g) under anesthesia by inhalation of a mixture of oxygen and halothane. Electrical self-stimulation (SS) in the median raphe of the rat but not in the locus coeruleus resulted in a dramatic rise of body temperature. Hyperthermia was facilitated by pretreatment with an inhibitor of serotonin uptake (3-(p-trifluoremethyl-phenoxy)-N-methyl-3-phenylpropylamine). The functional significance of the hyperthermia elicited by stimulation of the median raphe was discussed on the basis of the relationships between Ss and primary reinforcers. 10 references. (Author abstract modified)

000383 Miller, Robert E.; Deets, Allyn C. Department of Psychiatry, School of Medicine, Pittsburgh, PA 15261 **Delta-9-THC and nonverbal communication in monkeys.** Psychopharmacology (Berlin). 48(1):53-58, 1976.

The effect of delta-9-tetrahydrocannabinol (delta9-THC) on nonverbal communication is investigated monkeys trained to perform an instrumental avoidance conditioned response. Male rhesus preadolescent monkeys were paired in the cooperative conditioning paradigm, a situation designed to measure the quality of nonverbal communication by changes in facial expression. Oral administration of 1.0mg/kg of delta9-THC to the stimulus animal, the responder, both animals, or neither animal was given in all possible combinations of pairings to determine if delta9-THC affects the expressiveness of the responder to the expressions of others. The drug impaired the display of facial expression in stimulus subjects but enhanced the ability of responders to discriminate the expressions of their partners. Measures of heartrate during cooperative conditioning revealed that delta9-THC lowered cardiac rates of responder monkeys. 22 references. (Author abstract modified)

000384 Milloy, S.; Glick, S. D. Dept. of Pharmacology, Mount Sinai School of Medicine of the City University of New York, Fifth Avenue and 100th Street, New York, NY 10029 **Factors influencing tolerance to d-amphetamine-induced anorexia in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 221(1):87-95, 1976.

The relationship between development of tolerance to d-amphetamine induced anorexia and the experimental conditions under which it is studied was examined in rats. One group of rats on a 2 hr food deprivation schedule received d-amphetamine 15 min before eating every other day for a month. A second group of rats on a similar schedule received the same dose of drug immediately after eating. When compared to a saline treated control group, the first group showed significant decreases in weight and food intake on injection days. Tolerance to the amphetamine induced anorexia as demonstrated by an increase in weight occured after the fourteenth injection. The second group of rats showed a significant decrease in food intake on the non-drug days and an overall weight loss when compared to saline controls. In the second part of the experiment, treatment conditions were reversed, i.e. rats receiving d-amphetamine before eating received the drug after eating and vica versa. No overall weight loss occured at the end of the treatment period, indicating that tolerance to d-amphetamine induced anorexia is related to the duration of drug administration per se. The experiment was repeated with naive rats fed sweetened milk rather than the conventional pellets. Tolerance to the d-amphetamine develops after the 7th injection, showing that taste can be a factor in influencing the development of tolerance. It is concluded that both pharmacological and experimental factors play an important role in determining the rate of tolerance to d-amphetamine induced anorexia. 10 references. (Author abstract modifi ed)

000385 Milner, Joel S. Department of Psychology, Western Carolina University, Cullowhee, NC 28723 **Castration and amphetamine effects on acquisition of a Sidman avoidance task in rats.** Physiology & Behavior. 17(3):545-548, 1976.

An investigation was performed to determine whether the alterations in body chemistry produced by castration affect acquisition of a Sidman avoidance response, and to determine the effects of dextroamphetamine on acquisition of the task in castrated and sham operated rats. Castration inhibited acquisition of the task by both male and female animals. Amphetamine produced dose dependent differences in both response rates and shock rates. Low to moderate amphetamine doses facilitated acquisition, while higher doses were inhibitory. Response rates after facilitory doses of amphetamine were greater in sham operated animals than in castrated animals. 17 references. (Author abstract modified)

000386 Misslin, R.; Ropartz, P. Laboratoire de Psychophysiologie, Universite Louis Pasteur, 7, rue de l'Universite, D-67000 Strasbourg, Germany **Action of di-n-propylacetate on the spontaneous and acquired behaviour in goldfish, mice and rats.** Pharmacology Biochemistry and Behavior. 4(6):643-646, 1976.

The effects of n-dipropylacetate (nDPA) on spontaneous and conditioned behavior in 40 goldfish, 60 rats and 50 mice is described. The action of nDPA is related to the dose. In low doses, nDPA improved the number of conditioned responses with negative reinforcement. In higher doses, the drug inhibited spontaneous and conditioned behavior. As nDPA produces an increase in gamma aminobutyric acid (GABA) brain level, results are discussed in relation to the inhibitory action of GABA in the central nervous system. 12 references. (Author abstract modified)

000387 Moja, Egidio A.; Stoff, David M.; Gillin, J. Christian; Wyatt, Richard Jed. NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Dose-response effects of beta-phenylethylamine on stereotyped behavior in pargyline-pretreated rats.** Bethesda, MD, NIMH, 1976. 15 p.

Data are presented on the dose response and the time course effect of beta-phenylethylamine (4.0-64.0mg/kg i.p.)on stereotyped behavior and motor activity in male Sprague-Dawley rats pretreated 2 hrs earlier with pargyline (0.25-8.0mg/kg i.v.). Stereotyped behavior, defined as repetitive, nongoal directed head movements and sniffing, and changes in motor activity, were observed immediately after injection of beta-phenylethylamine for a 1 hr period. With increasing doses of pargyline pretreatment, beta-phenylethylamine produced, in a dose response relationship, progressively more stereotyped behavior accompanied by increased motor activity. Without pargyline pretreatment, only 64.0mg/kg beta-phenylethylamine induced behavioral changes. Stereotyped behavior and increased motor activity had an onset at 4-6 min after the injection of beta-phenylethylamine, peak at 10-30 min, and gradual decline in the next 10-20 mins. These results are discussed in terms of a possible relationship with the degree of inhibition of Type A and Type B monoamine oxidase caused by the different doses of pargyline. 31 references. (Author abstract)

000388 Monasmith, B.; Plotsky, P.; Blank, C. L.; Adams, R. N. Dept. of Chemistry, Univ. of Kansas, Lawrence, KS 66045 **The effects of 6-aminodopamine on electrical self-stimulation in rats.** Pharmacology Biochemistry and Behavior. 5(1):19-21, 1976.

Small doses of 6-aminodopamine (6-ADA), a powerful nervous system catecholaminergic neurotoxin, were injected intraventricularly in rats, and electrical self-stimulation (SS) in these rats was observed. These small doses of 6-ADA markedly depress electrical SS rates in rats. This 6-ADA treatment produced whole brain lowering of norepinephrine to approximately 50% of normal while the dopamine content was unchanged. The possible use of 6-ADA treatment to elucidate the relative roles of norepinephrine and dopamine pathways is discussed. 13 references. (Author abstract)

000389 Moore, Celia L. Department of Psychology, University of Massachusetts, Boston, MA 02125 **Experiential and hormonal conditions affect squab-egg choice in ring doves (Streptopelia risoria).** Journal of Comparative and Physiological Psychology. 90(6):583-589, 1976.

Noncycling, progesterone injected, experienced male ring doves prefer eggs to squabs in a simultaneous squab/egg choice test, while experienced male doves injected with both progesterone and prolactin prefer squabs to eggs. When exogenous prolactin is administered to either naive or experienced male ring doves during the early phase of a normal incubation cycle, squab choice is significantly increased. Squab choice is also significantly increased in incubating doves by 24 hr of exposure to a squab in the home nest. This effect is greater in naive than in experienced doves. Squabs introduced during late incubation have more of a positive effect on squab choice than when introduced during early incubation. It is concluded that intracyclic experience organizes successive behavioral changes within a reproductive cycle and that naive doves are more affected by some changes in intracyclic events than are experienced doves. 14 references. (Author abstract)

000390 Moreton, J. Edward; Roehrs, Timothy; Khazan, Naim. Department of Pharmacology and Toxicology, School of Pharmacy, University of Maryland, Baltimore, MD 21201 **Drug self-administration and sleep-awake activity in rats dependent on morphine, methadone, or l-alpha-acetylmethadol.** Psychopharmacology (Berlin). 47(3):237-241, 1976.

A study was conducted to examine the pattern of self-administration and the sleep/awake distribution within the interinjection intervals during dependence on methadone and l-alpha-acetylmethadol (LAAM) in comparison with morphine. Morphine postdependent rats were prepared with chronic cortical EEG electrodes, temporalis muscle EMG electrodes, and I.V. jugular cannulae, and permitted to self-administer morphine on a fixed ratio schedule of reinforcement to reestablish and maintain dependence. Morphine was then replaced by methadone or LAAM. The rats developed stable patterns of self-administration of each narcotic and maintained the dependent state. The distribution of sleep, REM sleep, and awakening within the interinjection interval for the three narcotics was similar. A short phase of behavioral stupor concomitant with EEG slow bursts emerged following the self-injections. This phase was followed by arousal with EEG activation. Sleep and REM sleep then reappeared and predominated before the next injection. LAAM manifested a relatively slow onset of action in comparison with morphine and methadone. 26 references. (Author abstract modified)

000391 Munkvad, I. Research Laboratories, Sct. Hans Mental Hospital DK-4000 Roskilde, Denmark **The mechanism of action of psychopharmacological agents on behaviour.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(Supplement 2):21-30, 1975.

The results of experimental animal studies and clinical work on the mechanism of action of psychopharmacological agents on behavior are presented. The problem of aggressiveness and abnormal social behavior is discussed from an anatomical, a behavioral and a biochemical point of view. The behavioral effects of amphetamines and neuroleptics on rats and several other laboratory animals are investigated. Clozapine, a new neuroleptic drug, is discussed as a strong antipsychotic with potential usefulness against psychotic aggressive behavior. The psychosis induced by amphetamines in men offers a model of schizophrenia that may in the future unlock the key to the mystery of what causes schizophrenia and other psychoses. 34 references.

000392 Nakamura, Mitsutaka; Fukushima, Hideaki; Kitagawa, Sumio. Research and Development Center, Pharmaceuticals Div., Sumitomo Chem. Co., Ltd., 4-2-1, Takatsukasa, Takarazuka, Hyogo 665, Japan **Effects of amitriptyline and isocarboxazid on 5-hydroxytryptophan induced head**

twitches in mice. Psychopharmacology (Berlin). 48(1):101-104, 1976.

Effects of amitriptyline and isocarboxazid on brain 5-hydroxytryptamine (5-HT) and 5-hydroxyindolacetic acid (5-HIAA) were examined in relation to their action on 5-hydroxytryptophan (5-HTP) induced head twitches. Amitriptyline reduced 5-HTP induced head twitches but isocarboxazid increased them. Both amitriptyline and isocarboxazid caused a significant increase of brain 5-HT concentration in 5-HTP treated mice. Amitriptyline also caused a significant increase of 5-HIAA concentration, while isocarboxazid reduced 5-HIAA concentration in the brains of 5-HTP treated mice. Probenecid, which significantly increased 5-HIAA concentration in 5-HTP treated mice, reduced 5-HTP induced head twitches. These results suggest that 5-HTP induced head twitches might be induced by an increase of 5-HT concentration, and reduced by an increase of 5-HIAA or a decrease of 5-HT concentration in the brains of mice. 15 references. (Author abstract)

000393 Nicholson, A. N.; Wright, Catherine M. Royal Air Force Institute of Aviation Medicine, Farnborough, Hampshire, England **Behavioural activity in the monkey (Macaca mulatta) of the metabolites of diazepam in man.** British Journal of Pharmacology (Basingstoke). 57(3):429P, 1976.

The effects of 1.8mg/kg and 3.0mg/kg doses of diazepam and its principal metabolites in man, i.e. N-desmethyldiazepam (nordiazepam), 3-hydroxydiazepam (temazepam) and 3-hydroxy-N-desmethyl-diazepam (oxazepam) on the ability of trained monkeys to perform delayed differentiation tasks and spatial delayed alternation tasks were investigated. Temazepam and oxazepam do not affect the performance of differentiation or alternation tasks. Both doses of diazepam and nordiazepam increase total response time in differentiation tasks 2 hours after administration but not 6 hours after administration. Diazepam impairs accuracy of response to matching on both GO and NO-GO responses. Both doses of diazepam impair performance of alternation tasks 2 hours after administration of the 3mg/kg dose only; impairment does not occur 4 hours or 6 hours after administration of a 3mg/kg dose. It is concluded that hydroxylation of a diazepam to temazepam or oxazepam is accompanied by a loss of activity or a considerable reduction in activity. Although activity persists after demethylation of diazepam to nordiazepam, it appears unlikely that the effects of diazepam are due solely to this metabolite. 4 references.

000394 Nieminen, L.; Mottonen, M. Pharmacological Laboratory of Research Center Laake-Medipolar, Turku, Finland **The pain aggression induced by bronopol in the rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 37(3):237-241, 1975.

Bronopol in doses of 7 to 25 mg/kg given intraperitoneally almost immediately releases a transitory aggressive behavior in rats. The painful state caused by bronopol induced chemical peritonitis probably brought about this behavioral phenomenon. The age of the animal and also the reserpine treatment play some role in this aggressive behavioral pattern. 12 references. (Author abstract)

000395 Ohtaka, Tadashi. Department of Neuropsychiatry, Tokyo Medical and Dental University, Tokyo, Japan **A neurophysiological study on the central action of psychotomimetics (LSD-25, DOM and ketamine).** Psychiatria et Neurologia Japonica (Tokyo). 76(2):103-128, 1974.

To investigate the neurophysiological basis of hallucination and dreamlike experiences, the effects of three different groups of psychotomimetics (LSD 25, DOM and ketamine) were studied by polygraphic recordings of EEG, eye movements and lateral geniculate PGO waves (GL wave), together with observations of general behavior in cats. LSD and DOM have a similar effect on the cats; excitation and inhibition appeared alternately with some inappropriate behavior noted. Ketamine induced a cataleptic anesthetic state. These three psychotomimetics showed common effects in the EEG of the animal including: the EEG of the neocortex showed various degrees of characteristic slowing, while EEG of the hippocampus showed relatively regular rhythmical theta waves similar to the hippocampal rhythmic waves. Referring to the reports of previous investigators on psychotomimetics and REM sleep, the implication of these findings is discussed from the viewpoint of hallucinogenesis and the appearance of dreamlike experience. 83 references. (Author abstract modified)

000396 Oka, Tetsuo; Hosoya, Eikichi. Dept. of Pharmacology, School of Medicine, Tokai University, Isehara, Kanagawa 259-11, Japan **The effect of p-chlorophenylalanine on the pethidine- or methadone-induced decrease in locomotor activity of rats.** European Journal of Pharmacology (Amsterdam). 37(2):393-395, 1976.

The way the serotonin modulator p-chlorophenylalanine acts on the decrease in locomotor activity induced in rats by narcotics other than morphine, such as pethidine and methadone, was studied. Either pethidine HCl (50mg/kg subcutaneously) or methadone HCl (8mg/kg subcutaneously) produced a prominent decrease in locomotor activity of rats. Pretreatment of rats with p-chlorophenylalanine (p-CPA, 320mg/kg interperitoneally) 48 hrs before the narcotic injection significantly antagonized the activity decreasing effects of narcotics. When rats pretreated with p-CPA were given 5-hydroxytryptophan (75mg/kg subcutaneously) 30 mins before narcotic administration, the activity decreasing response to narcotics was restored. Thus, a decrease in locomotor activity induced in rats by either pethidine or methodone is probably mediated by serotonergic mechanisms. 9 references. (Author abstract modified)

000397 Overton, Donald A.; Ercole, Mario A.; Dutta, Purabi. Department of Psychiatry, Temple Medical School, Philadelphia, PA 19140 **Discriminability of the postictal state produced by electroconvulsive shock in rats.** Physiological Psychology. 4(2):207-212, 1976.

Further investigations of the state dependent learning (SDL) effects of electroconvulsive shock (ECS) are reported, using a modified drug discrimination paradigm. Rats were trained to escape from shock in a T maze. Repeated training sessions were administered with a right return required after ECS and a left turn after no treatment. Experiments I and II were designed to measure the degree of postictal discriminability at different time intervals after ECS. Experiment III, an investigation to determine whether the discriminable effects of ECS and selected drugs (pentobarbital, scopolamine, physostigmine, carbacol and arecoline) were interchangeable in the drug discrimination paradigm. Experiment IV tested the combined effect of footshock and ECS. Results were as follows: 1) postictal state was readily discriminated 2-10 min after ECS; 2) discriminability attenuated by 60 min and was absent 2-7 days after ECS; 3) severe footshock just prior to ECS did not alter ECS discriminability; and 4) no simple interchangeability between cueing effects of drugs and ECS was found. The postictal state is discriminated as rapidly as are centrally

acting drugs. Similar mechanisms may be involved. 20 references.

000398 Page, J. G.; West, L. E. Eli Lilly and Company Toxicology Laboratories, Greenfield, IN 46140 **Acute tolerance to hypothermia in rats produced by d1-3-(1,1-dimethyl-heptyl)-6-alpha, beta,7,8,10a alpha hexahydro-1-hydroxy-6, 6-dimethyl-9H-dibenzo b,d pyran-9-one (Lilly compound 109514).** Pharmacologist. 17(2):211, 1975.

The effects of d1-3-(1,1-dimethylheptyl)-6 alpha,beta,7,8,10,10a alpha hexahydro-1-hydroxy-6,6-dimethyl-9H-dibenzo b,d pyran-9-one (Lilly compound 109514) on rectal temperature of the rat were investigated. Single oral doses of compound 109514 resulted in a marked hypothermia. The magnitude of the response was dependent on ambient temperature and persisted for more than 24 hr. The duration and magnitude of the hypothermic response was dose dependent. No hypothermic response occurred when a second dose was given 24 hr or 48 hr after the first dose, but the response occurred when a second dose was given 72 hr or more after the first dose. Animals given dimethylheptylpyran (DMHP) showed a similar hypothermia and tolerance to this response. A cross tolerance between DMHP and compound 109514 was demonstrated. Hypothermia was potentiated when theophylline or caffeine was administered prior to compound 109514. (Journal abstract modified)

000399 Palfai, Tibor; Albala, Bruce. Department of Psychology, Syracuse University, Syracuse, NY 13210 **Pentylenetetrazol - induced amnesia: a case for overt seizures.** Psychopharmacology (Berlin). 48(1):19-23, 1976.

The possible role of overt convulsions following pentylenetetrazol (PTZ) in retrograde amnesia was investigated in mice. Following a single passive avoidance conditioning, when overt convulsions were blocked with sodium pentobarbital (Nem), the amnesic effect of pentylenetetrazol was also blocked. Subconvulsive doses of the drug did not produce amnesia. Animals that received a typically convulsive dose of the drug but failed to convulse were not amnesic; only animals with overt convulsions were different from saline controls. The data suggest that overt convulsions may be necessary for the development of pentylenetetrazol induced retrograde amnesia. 14 references. (Author abstract)

000400 Parker, Lorne F.; Radow, Barbara L. Physiology-Psychology Group, Guthrie Hall, NI-25, University of Washington, Seattle, WA 98195 **Effects of parachlorophenylalanine on ethanol self-selection in the rat.** Pharmacology Biochemistry and Behavior. 4(5):535-540, 1976.

The efficacy of parachlorophenylalanine (PCPA), a tryptophan hydroxylase inhibitor that depletes the brain of serotonin in producing conditioned taste aversions and unconditioned avoidance of ethanol was investigated. Administration of PCPA to rats having free access to a saccharine solution and water produces aversions to saccharine that disappear within 6 days after termination of the PCPA treatments. Intraperitoneal injections of PCPA and/or ethanol given to rats not having access to ethanol produce no change in subsequent ethanol preferences. It is concluded that the capacity of PCPA to produce conditioned aversions to substances consumed during its administration is not specific for ethanol. It is also concluded that the ability of PCPA to cause consummatory aversions is the result of conditioning and does not depend on an interaction between the metabolism of the avoided substance and the serotonergic effects or other pharmacologic effects of PCPA. 17 references. (Author abstract modified)

000401 Peachey, J. E.; Rogers, B.; Brien, J. F.; MacLean, A.; Rogers, D. Addiction Studies Unit, Department of Psychiatry and Pharmacology, Queen's University, Kingston K7L 3K1, Canada **Measurement of acute and chronic behavioral effects of methamphetamine in the mouse.** Psychopharmacology (Berlin). 48(3):271-275, 1976.

A behavioral rating method and a data analysis procedure for the mouse in which the acute behavioral effects and chronic behavioral effects of dextromethamphetamine may be measured are described. Dose related behavioral responses occurring following acute dextromethamphetamine administration ranged from decreased quiescence through increased locomotor activity, a mixture of stereotyped behavior and increased locomotor activity to primarily stereotyped gnawing, licking or sniffing. Chronic administration of dextromethamphetamine produced more exaggerated behavioral responses than occurred with acute administration. In some animals, chronic treatment with 10mg/kg of the drug led to protracted self-tearing that replaced the gnawing, licking, sniffing stereotype. 14 references. (Author abstract modified)

000402 Plotnikoff, Nicholas P.; Kastin, Abba J. Endocrinology Section, Medical Service, Veterans Administration Hospital New Orleans, LA 70146 **Neuropharmacological tests with alpha-melanocyte stimulating hormone.** Life Sciences (Oxford). 18(11):1217-1222, 1976.

Neuropharmacological tests were conducted with the pituitary peptide hormone, alpha-melanocyte (MSH) to demonstrate its effects on behavior and central nervous system activity. Alpha-MSH was found to potentiate the behavioral effects of DOPA but not serotonin. It slightly reduced footshock induced fighting and decreased audiogenic seizures in susceptible mice, but was inactive in reducing the tremors induced by oxotremorine. The pattern of activity of alpha-MSH in these neuropharmacological tests differed from that of several other peptides. The results support the concept that naturally occurring peptides exert direct actions on the central nervous system independent of endocrine effects. 34 references. (Author abstract modified)

000403 Pohorecky, L. A. Rockefeller University, 1230 York Avenue, New York, NY 10021 **Withdrawal from ethanol: simple quantitative behavioral tests for its evaluation.** Psychopharmacology (Berlin). 50(2):125-129, 1976.

Several behavioral manifestations were evaluated in rats after withdrawal from ethanol following chronic administration. Compared with control animals, animals undergoing withdrawal displayed significant decreases in locomotor activity in a runway (indicated by the number of runs per trial and the time required to complete the first run), head poke activity, and rearing activity which persisted for 3 days to 5 days after termination of ethanol. It is suggested that behaviors such as these, which require no pretraining of animals, can be used to evaluate quantitatively the severity of withdrawal in rats. 16 references. (Author abstract modified)

000404 Poschlova, N.; Masek, K.; Krsiak, M. Institute of Pharmacology, Czechoslovak Academy of Sciences, Albertov 4, 128 00 Prague 2, Czechoslovakia **Facilitated intermale aggression in the mouse after 6-hydroxydopamine administration.** Neuropharmacology (Oxford). 15(7):403-407, 1976.

The effect of 5microgram and 50microgram doses of 6-hydroxydopamine on brain catecholamines and behavior of singly housed male mice on paired interactions with group housed partners was studied. 6-Hydroxydopamine produced a

significant and dose dependent depletion of noradrenaline and dopamine in the brain. No significant behavioral changes were found after 5microgram doses of 6-hydroxydopamine. The higher dose of 6-hydroxydopamine (50microgram) significantly increased the frequency of attacks, aggressive unrest and of tail rattles in the initially nonaggressive singly housed mice without changing their sociable, timid or locomotory activities. Significant negative correlations were found between the individual stimulation of aggressive activities and depletion of brain catecholamines. It is suggested that 6-hydroxydopamine can selectively facilitate intermale spontaneous aggression in the mouse. This facilitation seems to be related to the effect of 6-hydroxydopamine on catecholamine neurones. 25 references. (Author abstract modified)

000405 Pycock, C. Department of Neurology, Institute of Psychiatry, Denmark Hill, London SE5 8AF, England **Noradrenergic influences on dopamine-dependent behaviour in rats.** British Journal of Pharmacology (Basingstoke). 57(3):424P, 1976.

The effect of lowered cerebral noradrenaline levels on the behavior in rats characteristically observed after dopamine receptor stimulation and dopamine receptor blockade was studied. A reduction in cortical noradrenaline levels to about 40% to 50% of control levels was achieved in two separate groups of rats by injection of 6-hydroxydopamine at birth or by bilateral electrolesions placed in the region of the locus coeruleus in adult rats. The reduction in cerebral noradrenaline level has no effect on stereotyped behavior induced by either apomorphine or amphetamine, but it significantly enhances both the time to onset and intensity of catalepsy induced by haloperidol. It is possible that two different populations are responsible for the two types of behavior, and that each is modified by different noradrenergic mechanisms. 5 references.

000406 Randt, Clark T.; Samuels, Stanley; Fish, Irving Milbank Research Laboratories, Department of Neurology, School of Medicine, 550 First Avenue, New York, NY 10016 **Amino acid transport inhibition: brain and behavioral correlates.** Pharmacology Biochemistry and Behavior. 4(6):689-694, 1976.

Direct evidence of alteration of 14C-L-valine uptake by inhibitors of two enzymes in the gamma-glutamyl cycle in vivo and behavioral alterations in C57BL/6J mice are investigated. In vivo inhibition of uptake 14C-L-valine by brain following subcutaneous administration of either of two gama-glutamyl cycle enzyme inhibitors, 2-imidazolidone-4-carboxylic acid (ICA), or, L-methionine-S-sulfoximine (MSO) is documented in C57BL/6J mice. Dose related decrease in exploratory activity, impairment of memory for foot shock, and reduced operant responding for food reinforcement parallels the time course for interference with uptake of a large neutral amino acid by these two compounds previously shown to inhibit different enzymes in the gamma-glutamyl cycle subserving active amino acid transport. 40 references. (Author abstract modified)

000407 Rees, Howard D.; Dunn, Adrian J.; Iuvone, P. Michael. Department of Neuroscience, University of Florida College of Medicine, Gainesville, FL 32610 **Behavioral and biochemical responses of mice to the intraventricular administration of ACTH analogs and lysine vasopressin.** Life Sciences (Oxford). 18(11):1333-1340, 1976.

An experiment in which to determine behavioral and biochemical responses, adrenocorticatropic hormone (ACTH) 1-24, ACTH 4-10, ACTH 4-10 (D-phe), lysine vasopressin (LVP) or an amino acid mixture were administered to mice using bilaternal intraventricular injections is presented. Behavioral observations were made for the subsequent 85 mins, and the incorporation of subcutaneously injected (3H) lysine into brain proteins assayed for the last 10 mins of this period. Mice injected with ACTH1-24 showed the previously reported stretching and yawning syndrome, an effect also observed with ACTH4-10 (D-phe) but less often. These same peptides also induced a pronounced increase in the proportion of time mice spent grooming. LVP caused a dramatic hyperactivity. Mice so injected moved continously about the cage occasionally eating or grooming, but were never still. Injection with ACTH1-24 or ACTH4-10 (D-phe), but not ACTH4-10 or LVP, caused significant increases in the incorporation of (3H) lysine into brain protein. 23 references. (Author abstract)

000408 Rezek, M.; Havlicek, V.; Hughes, K. R.; Friesen, H. Department of Physiology, Faculty of Medicine, University of Manitoba, 770 Bannatyne Avenue, Winnipeg, Manitoba R3E OW3, Canada **Central site of action of somatostatin (SRIF): role of hippocampus.** Neuropharmacology (Oxford). 15(8):499-504, 1976.

The changes in behavior, motor coordination, sleep/waking cycle and electrical activity following the administration of various doses of somatotropin release inhibiting factor (somatostatin, SRIF) into two different loci of the hippocampal formation were investigated in the rat. The Direct Cerebral Administration of SIRF was characterized by several patterns of stereotyped behavior, alteration of the sleep/waking cycle and frequent dissociation of the EEG from behavior. Both behavioral and electrophysiological phenomena were found to be dose related. The administration of SRIF analogues via the same route failed to produce comparable effects, thus suggesting the specificity of SRIF action within the central nervous system. The results indicate that the hippocampus is involved in mediating the central, nonendocrine action of SRIF and are consistent with the hypothesis proposing the existence of a limbic pacemaker controlling stereotyped behavior. 31 references. (Author abstract modified)

000409 Rezek, Milan; Havlicek, Viktor; Hughes, Kenneth R.; Friesen, Henry. Dept. of Physiology, Faculty of Medicine, Univ. of Manitoba, Winnipeg, Manitoba, Canada **Cortical administration of somatostatin (SRIF): effect on sleep and motor behavior.** Pharmacology Biochemistry and Behavior. 5(1):73-77, 1976.

The effects of cortical administration of somatostatin (SRIF), one of the newly identified hypothalamic hormones, and its long-term influence on the sleep-waking cycle was studied in rats, and then, for a better assessment of the central effects of SRIF induced by systemic and direct cerebral administration of this hormone, SRIF was also adminitered intraperitoneally via chronic cannulas under the same experimental conditions as those for rats receiving cortical infusions. Cortical administration of SRIF in unrestrained, freely moving rats produced an early activation, stereotyped behavior patterns and later, coordination difficulties often associated with drowsiness. A few animals showed a tendency toward paraplegia in extension. A considerable, prolonged alteration in the sleep-waking cycle was also observed. Similar results were obtained in both intact and hypophysectomized animals. Intraperitoneal administration of SRIF induced several other effects in addition to those seen after cortical application. The latter were however, restricted in variety, intensity and duration. 13 references. (Author abstract modified)

000410 Rodgers, R. J.; Brown, K. Undergraduate School of Studies in Psychology, University of Bradford, Bradford BD7 IDP, Yorkshire, England **Amygdaloid function in the central cholinergic mediation of shock-induced aggression in the rat.** Aggressive Behavior. 2(2):131-152, 1976.

A series of experiments was designed to examine the role of central cholinergic mechanisms in shock induced aggression. Cholinergic blockade in the basolateral amygdala, ventral hippocampus, or dorsal hippocampus resulted in greatly reduced levels of fighting in response to footshock. However, while pain sensitivity remained unaltered in the amygdala group, both of the hippocampal groups exhibited decreased shock sensitivity. Further investigation of the amygdala revealed: 1) increased fighting in response to increased cholinergic levels; 2) neuroanatomical specificity to the basolateral division of this complex; 3) that an intact basolateral amygdala is essential to the normal manifestation of shock induced aggression; and 4) that social attraction remains unaltered by cholinergic blockade of the basolateral amygdala. Motor coordination and motor activity were not significantly affected in any treatment condition. 48 references. (Author abstract)

000411 Safta, L.; Cuparencu, B.; Sirbu, Aurelia; Secareanu, AL. Department of Pharmacology and Psychiatric Clinic of the Medical and Pharmaceutical Institute, Cluj - Napoca, Romania **Experimental observations on the effect of amphepramone on the behavior, locomotion, pentetrazol seizures and electroencephalogram.** Psychopharmacology (Berlin). 50(2):165-169, 1976.

The ability of amphepramone (diethylpropion) to produce amphetamine like CNS effects was investigated in mice, rats, and rabbits. Amphepramone produces hypermotility and stereotyped movements similar to those produced by amphetamine which can be antagonized with haloperidol. The doses of amphepramone required to produce the stereotyped behavior were larger than the anorectic doses. Amphepramone also potentiated the convulsant effect of pentetrazol and produced amphetamine like changes in the electroencephalogram. The stimulant activity of amphepramone observed in animals may explain the appearance in humans of a psychotic syndrome mimicking paranoid schizophrenia after ingestion of large doses of amphepramone. 19 references.

000412 Sahakian, Barbara J.; Robbins, Trevor W.; Iversen, Susan D. Department of Experimental Psychology, University of Cambrige, Cambridge, England **Alpha-flupenthixol-induced hyperactivity by chronic dosing in rats.** European Journal of Pharmacology (Amsterdam). 37(1):169-178, 1976.

The effects on locomotor activity of chronic administration of alpha-flupenthixol to developing socially reared and to isolation reared rats were studied. The effects of chronic apomorphine administration were studied for comparison. All animals treated chronically since weaning with alpha-flupenthixol show increased spontaneous locomotor activity compared with controls. Chronic apomorphine administration has no effect on spontaneous locomotor activity. Chronic alpha-flupenthixol treatment enhances stereotyped behavior occurring after 1.5mg/kg doses of dextro-amphetamine or 0.5mg/kg doses of apomorphine in the socially reared animals. Spontaneous stereotypes are also observed in the chronic alpha-flupenthixol treated rats. Chronic apomorphine treatment does not affect stereotyped responding. The results are discussed in terms of behavioral supersensitivity. It is suggested that the chronic treatment model described may prove interesting for comparing the various classes of antipsychotic drugs. 19 references. (Author abstract modified)

000413 Sanger, D. J.; Blackman, D. E. Department of Psychology, University of Birmingham, Birmingham, England **Schedule-controlled behaviour of rats as a technique for investigating the actions of benzodiazepines.** Bulletin of the British Psychological Society (London). 28:252, 1975.

Data are presented to illustrate the effects of chlordiazepoxide, a benzodiazepine drug, on patterns of operant behavior maintained in rats by various schedules of reinforcement. It is contended that the operant responding of rats can be suppressed during intermittent presentations of stimuli associated with the delivery of electric shocks. When benzodiazepines are administered to animals trained in such procedures, marked increases in suppressed responding are observed. Such effects have been interpreted as due either to a disinhibitory property of these drugs or to a general tendency for them to enhance low operant response rates. The results are discussed in the context of the two major interpretations. (Author abstract modified)

000414 Santacana, M. P.; Sanchez, E.; Munoz, M. C. Departamento de Biofisica, Centro des Investigaciones Biologicas, Velazquez, 144, Madrid-6, Spain **Effects of the administration of two doses of sulpiride on the behaviour of the rat.** Neuropharmacology (Oxford). 15(7):415-420, 1976.

The effect of intraperitoneal administration of 40mg/kg and 80mg/kg of sulpiride on the behavior of the rat was studied. At 40mg/kg, sulpiride acts as an anxiolytic agent since it slightly increases the exploration of the internal areas of the open-field, significantly decreases defecations, facilitates the approach to the goalbox in a conflictive situation and has no relevant effects on the acquisition and extinction of an active avoidance response. At the dose of 80mg/kg, a decrease in the exploratory behavior in the open-field (without an increment in defecations), an impairment in the acquisition and an irregular performance of the active avoidance response in the shuttlebox, and a decrease of intertrial responses in the shuttlebox occur. A recovery in the active avoidance response is observed when longer delays for response are allowed. The effects at the higher dose are different from those of neuroleptics and may be interpreted as due to a general depression on behavior. 33 references. (Author abstract modified)

000415 Schlemmer, R. Francis, Jr.; Casper, Regina C.; Siemsen, Frank K.; Garver, David L.; Davis, John M. Dept. of Pharmacology, College of Medicine, Univ. of Illinois Medical Center, Chicago, IL 60612 **Behavioral changes in a juvenile primate social colony with chronic administration of d-amphetamine.** Psychopharmacology Communications. 2(1):49-59, 1976.

Three selected members of a stable juvenile primate social colony of six, peer raised, one-year-old Stumptail macaques received 0.5mg/kg of d-amphetamine sulfate daily for four weeks. Amphetamine significantly reduced play activity to a minimum in the treated monkeys throughout the treatment period. These animals preferred huddling with eyes open, although no sedation was apparent. As the treatment period progressed, stereotyped behavior developed, rising significantly during the final week of treatment. This model may be useful in studying the seemingly "paradoxical" quietening effect of amphetamine in children. 7 references. (Author abstract)

000416 Schreiber, Henry L.; Wood, W. Gibson; Carlson, Richard H. Department of Psychology, Texas Tech University, P.O. Box 4100, Lubbock, TX 79409 **The role of locomotion in conditioning methylphenidate-induced locomotor activity.** Pharmacology, Biochemistry and Behavior. 4(4):393-395, 1976.

The hypothesis that overt performance of the entire response (actual running) is necessary for the conditioning of methylphenidate induced locomotor activity (wheel running) is tested. Four guinea-pigs were given daily injections of 2.5mg/kg methylphenidate (Ritalin) and were allowed to run in activity wheels; 4 other guinea-pigs were given methylphenidate and were placed in locked activity wheels; a third group of 4 guinea-pigs were administered saline and allowed to locomote; a fourth group of 4 guinea-pigs received saline injections and were placed in locked activity wheels. After 12 days of injection, all animals were given saline injections on the 9 subsequent days and allowed to run freely in the wheels. The 2 groups which had received methylphenidate showed more locomotor activity than the saline injected animals but were not distinguishable from each other on the basis of prior opportunity to engage in locomotor activity. These results were interpreted to indicate that (a) increased methylphenidate induced locomotor activity may be conditioned with repeated administration of the drug, and (b) actual running is not essential for the conditioning of drug induced wheel running. 14 references. (Author abstract modified)

000417 Schwartz, Arthur S.; Marchok, Patricia L. Division of Neurobiology, Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, Phoenix, AZ 85013 **Persistence of relapse of morphine-seeking behavior in rats: the relative role of certain biological variables.** Psychopharmacology (Berlin). 47(2):149-152, 1976.

The theory that narcotic induced protracted biological changes are responsible for relapse of opiate reinforced behavior was examined in the rat. Groups of rats were conditioned to prefer a distinctive environment by pairing it with morphine doses from 1-200mg/kg, and were retested for persistence of this preference after a 3 week abstinence period. They were then observed for protracted signs such as sensitivity to naloxone, tolerance to morphine analgesia, hyperaggression, or changes in endocrine activity. Acquisition and relapse of the preference, as well as long-term tolerance, were dose related. None of the purported protracted signs showed any consistent relationship to the tendency to relapse. However, relapse correlated significantly with original acquisition scores in all relapsing groups. The results suggest that original conditioning factors, rather than protracted biological changes, are responsible for the observed relapse. 19 references. (Author abstract)

000418 Segal, David S.; Geyer, Mark A. Psychiatry Department, UCSD School of Medicine, La Jolla, CA 92093 **Pre- and post-junctional supersensitivity: differentiation by intraventricular infusions of norepinephrine and methoxamine.** Psychopharmacology (Berlin). 50(2):145-148, 1976.

The mechanism by which intraventricularly administered 6-hydroxydopamine (6-OHDA) increases the behavioral response to infusion of norepinephrine (NE) was investigated in rats. Intraventricular infusions of methoxamine, an adrenergic agonist that has a relatively low affinity for the presynaptic uptake mechanism, produced a significant dose dependent increase in locomotor activity comparable to the increase elicited by infusion of equimolar doses of NE. The behavioral responsiveness to infusion of both NE and methoxamine was more than doubled 3 weeks after pretreatment with 6-OHDA. It is suggested that the increased responsiveness to NE induced by 6-OHDA is due to enhanced postsynaptic receptor sensitivity rather than to a loss of presynaptic uptake inactivation. 20 references. (Author abstract modified)

000419 Sell, Ari B.; Carlini, E. A. Universidade Federal de Santa Catarina, Rua Ferreira Lima 26 Centro Biomedico de Florianopolis, Santa Catarina, Brazil **Anesthetic action of methyleugenol and other eugenol derivatives.** Pharmacology (Basel). 14(4):367-377, 1976.

A comparative study of four natural eugenol compounds found in the volatile oil fraction of Myristica fragans, eugenol (E), methyleugenol (ME), isoeugenol and methylisoeugenol was carried out in mice. ME was also compared with pentobarbital and with the synthetic E derivative, propanidid, using the intraperitoneal route in rats. ME anesthetized the rats more rapidly then pentobarbital. The duration was the same. Propanidid was not active when injected through the intraperitoneal routes. Rats under ME anesthesia could be more easily operated, showed less cyanosis, and recovered better than those under pentobarbital. When injected i.v. in rabbits, ME and propanidid exhibited similar anesthetic effects. ME was shown to be nontoxic. Repeated injections sensitized the animals to the anesthetic action of ME. It was also found that ME was similar to pentobarbital in inducing large amounts of slow wave activity in EEG of rats and did not change the total brain levels of dopamine, norepinephrine and 5-hydroxytryptamine. It was concluded that ME has, in rats, an anesthetic action of short duration, which is at least comparable to, and probably better than that of pentobarbital. 20 references. (Author abstract modified)

000420 Senault, B. Departement de Pharmacologie, Laboratoire Le Brun, 41 bis, bd. Anatole-France, F-93300 Aubervilliers, France /**Aggressive behavior induced by apomorphine: relations with some elements of the behavioral profile and with the sensitivity to apomorphine.**/ Comportement d'agressivite a l'apomorphine: relations avec quelques elements du profil comportemental et avec la sensibilite a l'apomorphine. Psychopharmacology (Berlin). 48(1):31-35, 1976.

Apomorphine induced aggressive behavior in: rats is discussed in relation to some elements of the behavioral profile and to the sensitivity to apomorphine. Aggressive rats could be differentiated from nonaggressive rats on a lower rate of rearing reactions in the open field activity, as well as on a weaker aptitude for learning, increasing with the complication of the test. The two groups of rats had comparable activity, and a comparable response to pain. Apomorphine decreased the number of rearing reactions and defecations on open-field activity in the same manner in nonaggressive rats as in aggressive animals. In the usual housing conditions, apomophine increased similarly locomotor activity in both groups, but in observation cages of "emotional" type, the increase was much more pronounced in aggressive rats than in nonaggressive animals. 15 references. (Author abstract modified)

000421 Shannon, Harlan E.; Holtzman, Stephen G. National Institute on Drug Abuse, Division of Research, Addiction Research Center, Lexington, KY **Blockade of the discriminative effects of morphine in the rat by naltrexone and naloxone.** Psychopharmacology (Berlin). 50(2):119-124, 1976.

The capacity of naltrexone and naloxone to block the discriminative effects produced by morphine in the rat was evaluated using a two choice, discrete trial avoidance task. Both antagonists produced a dose dependent and time dependent blockade of morphine's effects. Naltrexone and naloxone were equipotent when given subcutaneously concomitantly with subcutaneously administered morphine. When the antagonists were given orally, naltrexone was more potent than naloxone, and had a longer duration of action. The discriminative effects

of morphine and methadone were compared after oral and subcutaneous administration. Both drugs produced dose related discriminative effects and were much less potent orally than subcutaneously. It is suggested that the discriminative effects produced by morphine in the rat can provide an animal model for the quantitative evaluation of antagonists that might be considered for use in maintenance programs for the treatment of narcotic addiction. 22 references. (Author abstract modified)

000422 Shaw, S. G.; Rolls, E. T. University of Oxford, Department of Experimental Psychology, South Parks Road, Oxford OX1 3UD, England **Is the release of noradrenaline necessary for self-stimulation of the brain?** Pharmacology, Biochemistry and Behavior. 4(4):375-379, 1976.

The hypothesis that a quantity of noradrenaline released contingently on every response made to obtain brain stimulation mediates the reward produced by the stimulation was tested. An alternative hypothesis is that reward is mediated by a different system, but that a steady activation of postsynaptic receptors by noradrenaline is necessary for normal behavior. The synthesis of noradrenaline was inhibited by disulfiram, and when lateral hypothalamic self-stimulation in the rat had ceased, alpha-adrenergic stimulants were injected intraventricularly (IC) or intraperitoneally (IP). The directly acting receptor stimulants oxymetazoline (0.9-250micrograms IC), naphazoline (20-250micrograms IC), and clonidine (0.75-3micrograms IC, 0.037-3mg/kg IP) did not restore self-stimulation, but the indirectly acting stimulants amphetamine (2mg/kg IP), methylphenidate (3mg/kg IP) and phenylephrine (15micrograms IC) did restore self-stimulation. In experiments 2 and 3, in which either the functional noradrenaline pool was depleted with disulfiram and amphetamine, or the reserve noradrenaline pool was depleted with reserpine, the action of phenylephrine in restoring self-stimulation was shown to be indirect, probably by mobilizing a reserve pool of noradrenaline. Because only indirectly acting noradrenergic stimulants which facilitate the release of noradrenaline restored self-stimulation, it is concluded that noradrenaline must be released contingent on every response for self-stimulation to occur. Whether this released noradrenaline mediates the reward or has some other function associated with bar-pressi ng behavior remains to be shown. 17 references. (Author abstract)

000423 Sheard, Michael H.; Davis, Michael. Yale University School of Medicine and Connecticut Mental Health Center, New Haven, CT 06508 **Shock elicited fighting in rats: importance of intershock interval upon the effect of p-chlorophenylalanine (PCPA).** Brain Research (Amsterdam). 3(2):433-437, 1976.

The effects of p-chlorophenylalanine (PCPA) on shock elicited aggression (SEA) in the rat was investigated. Intraperitoneal injection of PLPA enhances SEA when the intershock interval (ISI) is 15 sec but not when the ISI is only 3 sec. This difference cannot be accounted for by an effect on pain threshold since pain threshold is reduced by PEPA at both ISIs to a comparable degree. It is suggested that PCPA produces an increase in active avoidance behavior which interferes with its effect on SEA when the ISI is short but which dissipates sufficiently to permit the effect of PCPA on SEA to be detected when a longer ISI is used. 15 references.

000424 Siegel, R. K.; Johnson, C. A.; Brewster, J. M.; Jarvik, M. E. Department of Pharmacology, Univ. of California Los Angeles, Los Angeles, CA 90024 **Cocaine self-administration in monkeys by chewing and smoking.** Pharmacology, Biochemistry and Behavior. 4(4):461-467, 1976.

Two rhesus monkeys self-administered cocaine hydrochloride in a gum base vehicle on a fixed-ratio 10 schedule with performance characterized by frequent pauses and increased intertrial interval responding. Three other monkeys self-administered cocaine base in lettuce cigarette vehicles in smoking performance marked by shortened puff durations. Urinary benzoyl ecgonine levels correlated with amount of cocaine chewed or smoked. Monkeys did not prefer cocaine gum in choice tests with plain or procaine gum, but did significantly prefer cocaine cigarettes to plain cigarettes. These preliminary results emphasize the importance of route of administration in determining reinforcement efficacy of human coca use and suggest animal models for their further experimental analysis. 35 references. (Author abstract)

000425 Signorelli, Anthony. Psychology Department, Union College, Springfield Avenue, Cranford, NJ 07016 **Influence of physostigmine upon consolidation of memory in mice.** Journal of Comparative and Physiological Psychology. 90(7):658-664, 1976.

The influence of physostigmine upon the consolidation of memory was investigated in mice. Male mice of a DBA/2J strain were trained to escape shock in a Y-maze. Physostigmine (0.4mg/kg, i.p.)injected 2 days after initial learning impairs performance, but physostigmine injected 11 days after initial learning improves performance. The impairment of memory found 2 days after initial learning is transitory and is no longer evident once the drug is no longer active in the animal's system. The facilitation of performance found 11 days after initial learning is also transitory and is no longer evident once the drug is no longer active in the animal's system. It is suggested that an inhibitory hypothesis or a motivational hypothesis rather than a consolidation hypothesis is more appropriate for explaining the effects of physostigmine on task performance. 13 references. (Author abstract modified)

000426 Sofia, R. Duane; Knobloch, Linua C. Wallace Laboratories, Department of Pharmacology and Toxicology, Cranbury, NJ 08512 **Comparative effects of various naturally occurring cannabinoids on food, sucrose and water consumption by rats.** Pharmacology Biochemistry and Behavior. 4(5):591-599, 1976.

The effects of tetrahydrocannabinol (THC), cannabidiol (CBD), cannabinol (CBN), and d-amphetamine (d-AMP) on total caloric intake were studied in rats which had access to food and sucrose solutions as sources of calories as well as water for 6 hours each day. Three groups of rats were given the following dietary regimens: 1) water and dry food; 2) water, dry food, and 5% sucrose solution; 3) water, dry food, and 20% sucrose solution. Food and water consumption are dramatically reduced by each test drug immediately following and in some cases up to 4 days after intraperitoneal administration in all three groups. However, sucrose consumption is much less affected by each cannabinoid, indicating a preference for sweet calories, whereas d-AMP has an equal anorexic action on both food and sucrose consumption. It is suggested that THC, CBN, and CBD produce a preference for sweet calories in rats despite an overall anorexic effect. 17 references. (Author abstract modified)

000427 Springer, Alan D.; Schact, J.; Agranoff, B. W. Neurosciences Laboratory, University of Michigan, Ann Arbor, MI 48109 **The effect of memory blocking antibiotics and their analogs on acetylcholinesterase.** Pharmacology Biochemistry and Behavior. 5(1):1-3, 1976.

The ability of memory blocking antibiotics to inhibit acetylcholinesterase was measured in homegenates of goldfish

brain. Puromycin aminonucleoside was the most potent inhibitor followed by puromycin, cycloheximide and acetoxycycloheximide. Puromycin effectively impaired retention of active/avoidance learning in goldfish when injected either immediately before or after training, while puromycin aminonucleoside did not regardless of injection time. These results suggest that the known amnestic effects of puromycin, cycloheximide and acetoxycycloheximide are not a consequence of interference with acetycholinesterase. 10 references. (Author abstract)

000428 Stephens, D. N.; Franklin, K. B. J.; Herberg, L. J. Institute of Neurology, Queen Square, London WC1N 3BG, England **Differing but complementary functions of brain noradrenaline and dopamine in self-stimulation.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 266-270).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium in April 1975, support for a hypothesis which reconciles discrepant findings on the respective roles of noradrenaline (NA) and dopamine (DA) in intracranial self-stimulation (ICSS) is offered. The hypothesis proposes that both transmitters are essential and complementary, with NA mediating a response contingent reinforcing component, and DA maintaining a tonic state of motivation or arousal. The following specific predictions of the hypothesis were confirmed experimentally in rats: 1) d-amphetamine, which reportedly releases more DA than l-amphetamine, but not more NA, should be much more effective than l-amphetamine at NA sites; 2) thymoxamine HCl should attenuate reinforcement and depress SS at all sites, but especially at DA sites; 3) clonidine should depress SS at all sites; 4) apomorphine should be depressant at DA sites but stimulant at NA sites. These results are consistent with two component models of SS and suggest that the reinforcing components are noradrenergic and the motivating components dopaminergic. 3 references.

000429 Stewart, R. M.; Growdon, J. H.; Cancian, D.; Baldessarini, R. J. Psychiatric Research Laboratories, Massachusetts General Hospital, Boston, MA 02114 **5-Hydroxytryptophan-induced myoclonus: increased sensitivity to serotonin after intracranial 5,7-dihydroxytryptamine in the adult rat.** Neuropharmacology (Oxford). 15(8):449-455, 1976.

The effects of the serotonin precursor 5-hydroxytryptophan in rats previously treated with intracisternal injections of 5,7-dihydroxytryptamine (5,7-DHT) and systemic desmethylimipramine (DMI) were investigated. Tremor and myoclonus developed in animals pretreated with 5,7-DHT but not in control animals. The myoclonic syndrome was potentiated by pargyline, but was blocked by D-lysergic acid diethylamide (LSD), 2-bromolysergic acid diethylamide, methsergide, and centrally active high doses of the decarboxylase inhibitor, Ro4-4602. Drugs that increase or decrease the effects of other proposed central nervous system neurotransmitters (dopamine, norepinephrine, acetylcholine, and gamma-aminobutyric acid) neither reproduced the syndrome nor altered the myoclonus following 5-hydroxytryptophan. It is suggested that mycolonus induced by 5-hydroxytryptophan following treatment with 5,7-DHT and DMI appears to be specifically related to central indoleamine neurones and may reflect presynaptically or postsynaptically mediated supersensitivity to serotonin. 26 references. (Author abstract modified)

000430 Stewart, R. M.; Growdon, J. H.; Cancian, D.; Baldessarini, R. J. Psychiatric Research Laboratories, Massachusetts General Hospital, Boston, MA 02114 **Myoclonus after 5-hydroxytryptophan in rats with lesions of indoleamine neurons in the central nervous system.** Neurology. 26(7):690-692, 1976.

The neurologic consequences of administering 5-hydroxytryptophan (5-HTP) following the relatively selective lesioning of indoleamine neurons with a high dose of intracisternal 5,7-dihydroxytryptamine (5,7-DHT) after giving systemic desmethylimipramine (DMI) to protect norepinephrine neurons were investigated in rats. A myoclonic syndrome consisting of tremor, mycolonus and seizures is produced by injections of 5-HTP in the lesioned rats but not in controls. This behavioral response is blocked by pretreatment with the putative serotonin receptor blocking agents methysergide, lysergic acid diethylamide and bromolysergic acid diethylamide, as well as by centrally effective doses of the aromatic amino acid decarboxylase inhibitor R04-4602. Blockers of receptors of other neurotransmitters tested, including centrally active doses of phenoxybenzamine, propranolol, haloperidol, atropine and bicuculline, had little or no effect. It is suggested that this neurologic response in the adult rat may be relevant to some forms of clinical myoclonus in humans and that the testing method described may be useful in testing potential agonists and antagonists of serotonin receptors in the mammalian central nervous system. 16 references. (Author abstract modified)

000431 Strick, Peter L. Laboratory of Neurophysiology, National Institute of Mental Health, Bethesda, MD 20014 **Anatomical analysis of ventrolateral thalamic input to primate motor cortex.** Journal of Neurophysiology. 39(5):1020-1031, 1976.

The origin and topographical organization of input to the arm area of the primate motor cortex from the ventrolateral thalamus were examined using the method of retrograde transport of horseradish peroxidase (HRP). For simplicity the region containing labeled neurons has been termed the ventrolateral thalamic (VL) arm area. Injections of HRP into the somatic sensory cortex indicated that the thalmic regions which project to the somatic sensory cortex are separate from the VL arm area. The focal distribution of labeled thalamic neurons suggests that aspects of a point to point organization may exist in the connection between VL and the motor cortex arm area. The anatomical study was carried out in 8 monkeys. 61 references. (Author abstract modified)

000432 Su, Mei-Quey; Okita, George T. Department of Pharmacology, Northwestern University Medical School, Chicago, IL 60611 **Behavioral effects on the progeny of mice treated with methylmercury.** Toxicology and Applied Pharmacology. 38(1:):195-205, 1976.

The effects of prenatal methylmercury (MeHg) exposure on the behavior of postnatal offspring were determined in 129/SvSl mice. Results from the open-field test indicated that prenatal MeHg exposure decreases exploratory behavior as indicated by longer center square latency, lower number of peripheral squares traversed, lower frequency of backing, in treated groups in comparison to control groups. Depression in spontaneous locomotor activity was also observed in offspring prenatally exposed to MeHg; however, the effect diminished gradually as the animals grew older. In the flurothyl convulsion behavior test, it was found that animals prenatally treated with MeHg demonstrated significantly lower threshold to preliminary convulsion as well as maximal clonic-tonic convulsion; thus, indicating an increase in susceptibility to flurothyl induced convulsions. The observed decrease in exploratory behavior and spontaneous locomotor activity with an increase in convulsive susceptibility are not necessarily inconsistent

findings and may be due to MeHg affecting two independent mechanisms. Therefore, it has been demonstrated that behavioral effects can be induced in offspring prenatally exposed to MeHg. Furthermore, behavioral effects of MeHg can be detected in offspring having no detectable gross congenital malformations. 29 references. (Author abstract modified)

000433 Taillandier, Georges; Benoit-Guyod, Jean-Louis; Boucherle, Andre; Broll, Madeleine, Eymard, Pierre. Laboratoire de Chimie et Toxicologie, Groupe d'Etude et de Recherche des Medicaments, avenue de Verdun, 38240 Meylan, France **/Research in the dipropylacetic series. XII. Extended aliphatic acids and alcohols as anticonvulsants./** Recherches dans la serie dipropylacetique. XII. Acides et alcools aliphatiques ramifies anticonvulsivants. European Journal of Medicinal Chemistry (Paris). 10(5):453-462, 1975.

Former results obtained about 2-propyl pentanoic acid (dipropylacetic or DPA) were extended to other dialkylalkanoic acids having less than 14 carbon atoms and to some of their precursors (alcohols) or derivatives (amides). The effect of lengthening the chain bonding between the carbon bearing the two alkyl chains and the functional carbon on about 50 molecules is discussed. The anticonvulsant activity is improved in intensity and duration when lengthening that chain. Methods and materials used in testing for behavioral action, hypnotic action, anxiolytic action, antiaggressive action and antidepressive action are indicated. 29 references. (Author abstract modified)

000434 Taylor, M. Department of Psychology, Concordia University, Montreal, Quebec, Canada **Effects of L-tryptophan and L-methionine on activity in the rat.** British Journal of Pharmacology (London). 58(1):117-119, 1976.

The effects of an intraperitoneal dose of 20mg/kg L-tryptophan and doses of 100 and 150mg/kg of L-methionine were investigated on activity in the rat. Activity was measured by a time sampling behavior categorization procedure, and began 15 min after compound administration lasting for a total of 1 hour. Total active behavior in the first half hour was reduced after 20mg/kg tryptophan, 100 or 150mg/kg methionine. Only 20mg/kg tryptophan led to a significant reduction in active behavior during the second half hour. Administration of 100mg/kg tryptophan had no discernible effect on activity. It is concluded that the role of another amino acid in the modification of the behavioral effects of tryptophan is indicated. 16 references. (Author abstract modified)

000435 Telner, John I.; Vikis-Freibergs, Vaira; Lepore, Franco. Departement de Psychologie, Universite de Montreal, C.P. 6128, Montreal 101, P.Q., Canada **Effects of low and moderate doses of chlorpromazine on discrimination learning in the rat.** Psychopharmacology (Berlin). 47(2):205-208, 1976.

The effects of chlorpromazine (CPZ) on the acquisition of a brightness discrimination with food reward were examined. Doses of CPZ as well as saline were administered intraperitoneally to four groups of seven Sprague-Dawley rats, 1 h prior to testing. After a 3 week period of habituation and pretraining, rats were tested 20 trials a day, 7 days a week. No drug effect was found on the number of trials to reach a criterion of 18/20 successive correct responses, which required an average of 6.2days of training. Precriterion latencies, however, showed an increase as a function of increasing dose level. Postchoice latencies were not affected, eliminating motor retardation as an explanation for the latency effect. A few studies remain in which, contrary to the present findings and several others, responding to the incorrect stimulus was actually found to increase under CPZ. Since drug effects in the Terrace study (using pigeons as Ss) were dependent on the method of learning (with or without errors), this variable requires further investigation. Therefore, current research is attempting to establish errorfree discrimination in the rat, in order to verify the generality of Terrace's findings. 21 references. (Author abstract modified)

000436 Thomas, John R. Behavioral Sciences Department, U. S. Naval Medical Research Institute, Bethesda, MD 20014 **Interaction between hyperbaric air and d-amphetamine effects on performance.** Psychopharmacology (Berlin). 48(1):69-73, 1976.

The effects of amphetamines on behavior under hyperbaric conditions were investigated. Rats performing on a progressive ratio schedule that required five additional responses for each successive food reinforcement were administered d-amphetamine. The number of responses required increased until the next ratio was not completed within 15 min. The number of reinforcements obtained during a session increased with strengthened doses of d-amphetamine from 0.25mg/kg to a maximum behavioral effect at 1.0to 2.0mg/kg followed by a decline with higher doses. To assess the effects of hyperbaric air on the established d-amphetamine performance, the same doses were administered to rats breathing compressed air at seven times normal atmospheric pressure (7.1ATA). In the hyperbaric condition the dose/effect function was displaced toward smaller doses such that the maximum behavioral effect was obtained at lower doses than under normal atmospheric pressure; doses that produced maximum behavioral effects under normal pressure produced a decline in reinforcements obtained. 13 references. (Author abstract modified)

000437 Thompson, Donald M. Department of Pharmacology, Georgetown University, Schools of Medicine and Dentistry, Washington, DC 20007 **Repeated acquisition of behavioral chains: effects of methylphenidate and imipramine.** Pharmacology Biochemistry and Behavior. 4(6):671-677, 1976.

A method involving repeated acquisition of behavioral chains was used to assess the effects of methylphenidate and imipramine in individual animals. Pigeons obtained food for completing a 4-response chain, which was changed from session to session. Learning was defined by the decrease in errors across trials within a session; overall accuracy was measured by total errors per session. For comparison, the drug tests were also conducted under a performance condition, in which the 4-response chain was the same from session to session. In general, both drugs increased total errors per session as a function of dose under both the learning and performance conditions. The error increasing effect was greater with imipramine than with methylphenidate and was detected at lower doses under the learning condition than under the performance condition. Under the learning condition, the higher doses of both drugs decreased the rate of within session error reduction. Neither drug enhanced accuracy at any of the doses tested. The lower doses of methylphenidate slightly decreased total trial time under both the learning and performance conditions. 20 references. (Author abstract)

000438 Thornburg, J. E.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Supersensitivity to dopaminergic agonists induced by haloperidol.** In: Bernard, B., Aminergic hypotheses of behavior: reality or cliche? Rockville, MD, National Institute on Drug Abuse, 1975. 149 p. (p. 23-28).

Haloperidol caused a significant reduction in the spontaneous locomotor activity of mice when added to their diet for 11

days, and upon removal of the drug from their diet these mice exhibited withdrawal hyperactivity for several days that was characterized by an increase in activity over control or prehaloperidol values. Similar results were obtained when mice were fed a diet containing pimozide. Withdrawal hyperactivity was not detected after 1 or 3 days of a haloperidol containing diet, but was maximal after 6 days of this diet. Dose response curves of apomorphine stimulated motor activity and rearing behavior were shifted to the left when determined in mice during the period of withdrawal hyperactivity. Dopaminergic agonists (apomorphine, piribedil, L-DOPA and d-amphetamine) induced gnawing at lower doses in mice removed from a chronic haloperidol containing diet for 2 days than in mice maintained on a control diet. These results support the hypothesis that prolonged blockade of central dopaminergic receptors by neuroleptics cause subsequent behavioral effects that may be due to the development of enhanced receptor sensitivity. 23 references. (Author abstract)

000439 Tinklenberg, Jared R.; Gillin, J. Christian; Murphy, Greer M., Jr.; Wyatt, Richard J. Department of Psychiatry, Stanford Medical Center, Stanford, CA 94305 **Phenylethylamine effects in rhesus monkeys (unpublished paper).** Bethesda, MD, NIMH, 1976. 1 p.

The effects of phenylethylamine (PEA), a noncatecholamine biogenic amine with possible implications in affective disorders, schizophrenia and other paranoid psychoses, was assessed in rhesus monkeys. Emphasis was on its role in inducing stereotyped psychotic behavior. Single injections produced dose related (25-75mg/kg) significant increases in checking and lip smacking, as well as decreases in goal directed behaviors such as grooming. These effects were maximal at 15 min postinjection, still substantial at 30 min, and mostly dissipated at 60 min. Pretreatment with alpha-methyl-para-tyrosine (ampT), but not with phenobarbital substantially reduced these effects. When the pretreatment was followed by a subthreshold dose of L-dopa, effects were restored, suggesting that at least some PEA effects require intact dopaminergic mechanisms, and that ampT does not block PEA receptors. The behavioral effects in rhesus monkeys of the endogenous substance, PEA, suggest that it may provide a useful animal model of psychosis.

000440 Tremain, James Edward. Arizona State University, Tempe, AZ 85281 **Effects of anticholinergic agents on conditioned inhibition in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-9167 HC$20.00 MF$10.00 87 p.

Three experiments examined the effects of centrally and peripherally active anticholinergic agents (scopolamine and methyl-scopolamine) on a water reinforced discrimination operant task. Subjects were trained then tested following one of three drug injections: saline, methyl-scopolamine, or scopolamine. Subjects were found to respond most to the S+ cue and least to the S-minus cue. Subjects trained following injections of saline were found to respond significantly less during the combined cue test after injections of scopolamine than after injections of saline. Yet, subjects trained following injections of scopolamine were found to respond significantly less during the test after injections of the saline than after injections of scopolamine. Therefore, the results appeared to be due to a state dependency effect. Thus, the study failed to support the hypothesis that centrally active anticholinergic agents block conditioned inhibition. (Journal abstract modified)

000441 Trulson, Michael E.; Eubanks, Edwin E.; Jacobs, Barry L. Department of Psychology, Princeton University, Princeton, NJ 08540 **Behavioral evidence for supersensitivity following destruction of central serotonergic nerve terminals by 5,7-dihydroxytryptamine.** Journal of Pharmacology and Experimental Therapeutics. 198(1):23-32, 1976.

A complex behavioral syndrome, consisting of tremor, rigidity, hindlimb abduction, Straub tail, lateral head weaving, and reciprocal forepaw treading, was utilized to test for supersensitivity in the central serotonergic system in rats. Specific destruction of central serotonin nerve terminals by intraventricular injection of 5,7-dihydroxytryptamine (5,7-DHT) in adult male rats pretreated with a catecholamine uptake blocking agent resulted in marked supersensitivity to serotonin precursors and agonists. The greatest degree of supersensitivity was observed in response to L-5-hydroxytryptophan, for which the ED50 for elicitation of the syndrome was 20% of the value for control rats. A lesser degree of supersensitivity was seen in response to L-tryptophan (following monoamine oxidase inhibition) and the direct acting serotonin agonist, 5-methoxy-N,N-dimethyltryptamine, for which the ED50 was approximately 50% of the control value in both cases. Supersensitivity begins to develop within 24 hours and is relatively complete by 96 hours after 5,7-DHT. A marked subsensitivity to the serotonin releasing agent, fenfluramine, was found in 5,7-DHT treated rats. In contrast to the marked supersensitivity to serotonin precursors and agonists which occurs following 5,7-DHT, chronic administration of a serotonin synthesis inhibitor, p-chlorophenylalanine (400mg/kg every 3 days for a total of 24 days), did not produce supersensitivity to L-5-hydroxytryptophan or 5-methoxy-N,N-dimethyltryptamine. Possible pre and postsynaptic mechanisms for the development of supersensitivity are discussed. 51 references. (Author abstract modified)

000442 Turner, Evelyn G.; Altshuler, Harold L. 11550 Chimney Rock, No. 303, Houston, TX 77035 **Conditioned suppression of an operant response using d-amphetamine as the conditioned stimulus.** Psychopharmacology (Berlin). 50(2):139-143, 1976.

The use of a drug state as a conditioned stimulus (CS) in a classical conditioning paradigm was investigated in rats. Suppression of a single lever food reinforced response served as an index of a classically conditioned response (conditioned suppression). Following pairing of d-amphetamine injections with inescapable electric shocks, the effects of d-amphetamine on operant response totals were compared to effects obtained in control subjects which had received unpaired d-amphetamine and shock exposure. d-Amphetamine administered during operant sessions unaccompanied by shock was an effective CS for conditioned suppression of the operant response. Administration of cocaine hydrochloride also produced a decrease in total responses, suggesting stimulus generalization from the shock paired drug to a novel drug. 23 references. (Author abstract modified)

000443 van Riezen, H.; Schnieden, H.; Wren, A. Department of Pharmacology, Metaria Medica and Therapeutics, University of Manchester, Manchester M13 9PT, England **Behavioural changes following olfactory bulbectomy in rats: a possible model for the detection of antidepressant drugs.** British Journal of Pharmacology (Basingstoke). 57(3):426P, 1976.

The effects of subchronic treatment with amitriptyline, Org GB 94, chlorpromazine, chlordiazepoxide, dextroamphetamine, and lithium sulfate (SO rats) on rats subjected to either olfactory bulbectomy (OB rats) or to sham

operation were investigated in order to determine whether the reversal by amitriptyline of behavioral deficits resulting from bulbectomy occurs with all antidepressants. Amphetamine increases, but chlorpromazine and chlordiazeposide decrease, open-field activity in control as well as in OB rats. The antidepressants, and to a lesser extent lithium, reduce activity in OB rats but have little effect on SO rats. Bulbectomy produces deficient acquisition of appetite motivated behavior and avoidance behavior and the antidepressants reverse this deficit. However, they worsen the performance of the SO rats. A similar result is obtained with rats treated with amphetamine but not with those treated with chlorpromazine, chlordiazepoxide, or lithium. It is concluded that the procedure described is useful in differentiating between antidepressants and other psychotropic compounds. 5 references.

000444 Vincent, John H.; Lenzer, Irmingard I. Saint Mary's University, Halifax, Nova Scotia, Canada, B3H 3C3 **Effects of 2,5-dimethoxy-4-methylamphetamine (DOM, STP) on successive sensory discrimination behavior maintained by electrical stimulation of the brain reinforcement in the rat.** Psychological Reports. 38(3):1083-1092, 1976.

The effects of 2,5-dimethoxy-4-methylamphetamine (DOM) on behavior reinforced by electrical stimulation of the brain were observed in five male Sprague-Dawley rats. The animals were trained on a successive discrimination task: the S(D) interval lasted as long as it took the animal to make one lever press; the S(delta) interval was variable, with a mean duration of 60 sec. Following DOM administration, response latencies to the S(D) were longer during the first 75 min and S(delta) responding was augmented over the 2 hr session. Gross behavioral effects such as hypokinesia and ataxia were observed for a large part of the session. While increased response latencies may be attributed to hypokinesia and ataxia, increases in S(delta) responding reflect a breakdown of discrimination itself. Severe behavioral depression was not observed, suggesting that electrical stimulation of the brain may have counteracted the depressive effect of the amphetamine. 18 references. (Author abstract)

000445 Wahlstrom, Goran. Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden **The interaction between electrically induced convulsions and tolerance in the abstinence period after chronic barbital treatment in the rat.** Psychopharmacology (Berlin). 48(3):239-245, 1976.

The effect of electrically induced convulsions on tolerance to hexobarbital after chronic barbital treatment was studied in rats. Tolerance was tested on the 3rd day and on the 24th day after discontinuation of the barbital with an EEG threshold method in which hexobarbital was infused intravenously to obtain a criterion of burst suppression. Electrically induced convulsions produced 1 hr prior to threshold determination decreased the hexobarbital threshold when compared with barbital treated animals in which no convulsion was produced. Hexobarbital thresholds in control animals were not influenced by induction of a convulsion. Threshold was not increased on the 24th abstinent day, suggesting that induction of a convulsion which influences tolerance to hexobarbital after chronic barbital treatment may have long-term effects in rats. The hypothesis that convulsions after barbiturate withdrawal represent physical dependence is not refuted. 24 references. (Author abstract modified)

000446 Wei, Eddie. Department of Biomedical and Environmental Health Sciences, School of Public Health, University of California, Berkeley, CA 94720 **/Shaking behavior induced by AG-3-5 in several criminal species./** no title. Psychopharmacology Bulletin. 12(3):3-4, 1976.

It is reported that oral or parenteral AG-3-5 causes fur bearing animals (mice, rats, gerbils, hamsters, guinea pigs, rabbits, cats and dogs) to shake like a wet dog trying to remove water from its back. The shaking produced by this compound is suppressed by opiates and by clonidine but is only partially attenuated by pharmacologically active doses of neuroleptics and barbiturates. Because thyroid releasing hormone (TRH) and opiate antagonists also produce similar shaking, it is suggested that AG-3-5 should be considered for evaluation as a psychoactive drug, although the theoretical implications of shaking behavior to CNS processes are not clear. 6 references.

000447 Wei, Eddie; Loh, Horace. Department of Biomedical and Environmental Health Services, School of Public Health, University of California, Berkeley, CA 94720 **Physical dependence on opiate-like peptides.** Science. 193(4259):1262-1263, 1976.

Methionine enkephalin and beta-endorphin, endogenous peptides with activities similar to those of opiates, were infused for 70 hours into the periaqueductal gray fourth ventricular spaces of the rat brain. When challenged with a naloxone, a specific opiate antagonist, these animals manifested a typical morphine like withdrawal syndrome. These results show that such peptides can cause physical dependence. It is concluded that methionine enkephalin and beta-endorphin can cause morphine like physical dependence. The potent activity of beta-endorphin in producing dependence suggests that mechanisms of physical dependence may regulate the actions of this peptide in vivo. 15 references. (Author abstract modified)

000448 Weiner, William J.; Goetz, Christopher; Klawans, Harold L. Neurology Dept., Naval Hospital, Memphis, Millington, TN **Serotonergic and antiserotonergic influences on apomorphine-induced sterotyped behaviour.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(2):155-160, 1976.

The possible role of serotonin in modifying apomorphine induced behavior was investigated by studying the effects of methysergide and 5-hydroxytryptophan on the threshold dosage of apomorphine required to induce stereotyped behavior. The central serotonin antagonist methysergide potentiated apomorphine induced stereotyped behavior, and 5-hydroxytryptophan, the precursor of serotonin, inhibited apomorphine induced stereotyped behavior. These results suggest that serotonin may play a role in the balance of neurotransmitters within the striatum that influence movements. 19 references. (Author abstract)

000449 Weisz, Donald J.; Vardaris, Richard M. Kent State University, Kent, OH 44242 **Effects of delta-9-tetrahydrocannabinol on the slope of auditory generalization gradients in rats.** Physiological Psychology. 4(2):145-148, 1976.

Groups of rats were given 2, 4, or 6mg/kg delta-9-tetrahydrocannabinol (THC) to test its effects during shuttle avoidance training and auditory generalization testing in extinction. Although the drug had no discernible effect on acquisition performance, there was a does dependent influence on the slopes of the generalization gradients. It was concluded that THC can affect the extent of auditory generalization during extinction, even when there is no apparent effect on acquisition performance. The outcomes of the study were interpreted in terms of their relevance to the drug's presumed effects on audition and various motivational processes. 12 references. (Author abstract)

000450 Werboff, Jack; Ross, Sherman; Hayhurst, Viola F. University of Connecticut Health Center, Storrs, CT 06268 **Food dominance in dogs: effects of chlorpromazine and d-amphetamine.** Psychological Reports. 38(3):1287-1291, 1976.

Effects of chlorpromazine and d-amphetamine on food dominance were studied in 18 purebred dogs over a 10 week period. Dominance was determined by time spent at a common food dish. Trials were conducted each week with no drugs to determine the dominance relationships, followed by each dominant and submissive member receiving either saline, d-amphetamine, or chlorpromazine. New pairings were created on the following week with a total of 72 pairings and 144 drug treatments. Dominance (dominant or submissive) was a function of particular pairings. Amphetamine altered dominance relationships only when administered to the dominant animal. Chlorpromazine altered the dominance relationship only when administered to the submissive animal. 3 references. (Author abstract)

000451 Wilson, Linda M.; Riccio, David C. Dept. of Psychiatry, Mental Health Research Institute, Univ. of Michigan, Ann Arbor, MI 48109 **Scopolamine's effect on passive avoidance behavior in immature rats.** Developmental Psychobiology. 9(3):245-254, 1976.

Male albino rats ranging in age from 15-30 days were injected with either scopolamine hydrobromide or saline, prior to training and retention testing on a black/white passive avoidance (PA) task. Pretraining administration of a 1.0mg/kg dose of scopolamine significantly increased the median number of trials to criterion for 18, 21, and 30-day-old rat pups when compared with their saline controls. Fifteen day olds showed drug related PA deficits when a 2.0mg/kg dose was given. Retention data reflect characteristic age dependent memory loss over the 1 week acquisition retention period with no apparent state dependent effects. The data suggest the presence of cholinergic inhibitory mediation of PA responding in preweanling and postweanling pups. 30 references. (Author abstract)

000452 Wilson, T. R. Department of Pharmacology, Manchester University, Manchester, England **Effects of benzodiazepine tranquillizers on the social responses of rats.** Bulletin of the British Psychological Society (London). 28:258, 1975.

The effects of benzodiazepine tranquilizers on the social behavior of five male hooded Wistar rats were investigated to further determine the effects of group size and composition on reaction to psychotropic drug administration. Administration of chlordiazepoxide, diazepam and medazepam significantly depressed gross motor activity, exploratory and emotional behavior of the five hooded rats on their own. When rats with whom they had earlier been grouped were reintroduced to them, there occurred an increase in activity in the drug treated rats which not only completely offset the depressant actions of the drug, but increased the activity over normal control values. Introduction of stranger animals (albino Wistar rats) to the hooded rats partly offset the decrease in activity brought about by the drug. The drugs significantly reduced the usual reactions of the hooded rats to albino strangers. Reductions in activity were dose related, and indicated in this regard a potency relationship: medazepam to diazepam to chlordiazepoxide. Although these results are clearly related to the ability of drugs of this type to reduce the emotional response of the hooded rats to strangers, there must also be taken into account the effects of social facilitation occurring in the experimental situation. 4 references. (Author abstract)

000453 Woodruff, Michael L.; Hatton, Daniel C.; Frankl, Matt B.; Meyer, Merle E. Department of Psychology, Middlebury College, Middlebury, VT 05753 **Effects of scopolamine and physostigmine on tonic immobility in ducks and guinea pigs.** Physiological Psychology. 4(2):198-200, 1976.

The present study was performed to test the effects of the anticholinergic drug scopolamine and the cholinergic potentiating drug physostigmine on tonic immobility (TI) in ducks and guinea-pigs. Scopolamine shortened the duration of the response in ducks, while increasing TI duration in guinea-pigs. Physostigmine, on the other hand, increased TI duration in ducks, while shortening the response in guinea-pigs. Though the neurochemical systems mediating the response may differ, it is suggested that TI could serve as a useful model behavior for studying functional homology between the brains of birds and mammals. 11 references. (Author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

000454 Alhava, Eeva; Rutanen, Sirkku; Attila, Martti. Department of Pharmacology, School of Pharmacy, University of Helsinki, Kirkkokatu 20, SF-00170 Helsinki 17, Finland **Toxicity and temperature responses induced by d-amphetamine and cocaine in developing mice.** Acta Pharmacologica et Toxicologica (Kobenhavn). 39(1):141-144, 1976.

The effect of the blockade of monoamine reuptake on amphetamine induced responses was studied in relation to age in mice. Toxicity (as determined by mortality rate) and effect on body temperatures of d-amphetamine and cocaine, alone and in combination, was observed after intraperitoneal injection into adults and developing mice (aged 13 to 16 days). Amphetamine is more toxic to adult than to developing mice, while cocaine is more toxic to developing mice than to adults. In developing mice, pretreatment with 30mg/kg of cocaine increases the toxicity of 20mg/kg of amphetamine. In adults, cocaine slightly augments the amphetamine toxicity, but the difference is not significant. Amphetamine produces hyperthermia in adult mice. In developing mice, 20mg/kg of the drug produces pronounced hyperthermia, 50mg/kg produces a slight increase in temperature, and 100mg/kg produces a pronounced hypothermia. Cocaine does not produce significant changes in body temperature in adult mice; in developing mice, cocaine produces hypothermia. In adult mice, pretreatment with cocaine attenuates the hyperthermia produced by amphetamine. In developing mice, the hyperthermia produced by 20 mg/kg of amphetamine is prolonged after pretreatment with cocaine. It is suggested that the monoamine reuptake mechanisms of developing neuronal membrane are more sensitive to blocking agents than those of adult animals. However, potentiation by cocaine of amphetamine toxicity in developing mice implies the existence of relatively responsive catecholamine receptors in the developing mouse brain. 6 references.

000455 Beaubien, A. R.; Carpenter, D. C.; Mathieu, L. F.; MacConaill, M.; Hrdina, P. D. Drug Toxicology Division, Health Protection Branch, Tunney's Pasture, Ottawa K1A 0L2, Canada **Antagonism of imipramine poisoning by anticonvulsants in the rat.** Toxicology and Applied Pharmacology. 38(1):1-6, 1976.

A study was undertaken to determine which of the anticonvulsants, diazepam, phenobarbital, and phenytoin, was most efficacious in reducing imipramine induced convulsions in rats. Dose response curves were obtained in male Wistar rats for imipramine induced convulsions and death. For ip administration, the median convulsive dose (CD50) was only slightly

lower that the LD50. The calculated LD90 was used to test the effectiveness of diazepam, phenytoin, or phenobarbital in preventing imipramine seizures. Imipramine convulsions could be prevented by either diazepam or phenobarbital but not by phenytoin. The ip median preventive dose (PD50) for diazepam was estimated to be 0.32mg/kg, and for phenobarbital, 17.6mg/kg. 23 references. (Author abstract modified)

000456 Boddy, K.; Dawes, G. S.; Fischer, R. L.; Pinter, S.; Robinson, J. S. Simpson Memorial Pavilion, Royal Infirmary, Edinburgh, Scotland **The effects of pentobarbitone and pethidine on foetal breathing movements in sheep.** British Journal of Pharmacology (London). 57(2):311-317, 1976.

Small doses of pentobarbitone (4mg/kg i.v.)administered to sheep in the last trimester of pregnancy have little overt effect on the mothers; however, in the fetus they cause arrest of breathing movements, an alteration in the character of the electrocorticogram and cardiovascular changes which vary with gestational age. In contrast, relatively large doses of pethidine (100-200mg) administered to the mother have no consistent effect on normal fetal breathing movements, though they abolish the fetal response to hypercapnia. The results are discussed in relation to fetal sleep state. 27 references. (Author abstract)

000457 Bodin, Nils-Olof; Flodh, Hans; Magnusson, Goran; Malmfors, Torbjorn; Nyberg, Jan-Anders. Toxicology Laboratories, Astra Pharmaceuticals AB, S-151 85 Sodertalje, Sweden **Toxicological studies on metoprolol.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):96-103, 1975.

A review of the toxicological studies in animals on a cardioselective beta-blocking agent, metoprolol, is presented. Studies after single administration were performed in mice, rats and dogs. LD50-values were calculated for rodents while maximum tolerated dose was estimated for dogs. Studies after repeated administration for up to 6 months were performed in rats and dogs; reproduction studies were performed in rats and rabbits. Results indicate no toxic effect using metoprolol other than acute effects observed after single, high dose experiments. 2 references. (Author abstract modified)

000458 Elonen, E.; Linnoila, M.; Lukkari, I.; Mattila, M. J. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Concentration of tricyclic antidepressants in plasma, heart and skeletal muscle after their intravenous infusion to anaesthetized rabbits.** Acta Pharmacologica et Toxicologica (Kobenhavn). 37(4):274-281, 1975.

In order to compare the toxic concentrations of 4 different tricyclic antidepressants in the heart and plasma, 5mg/kg of amitriptyline, doxepin, nortriptyline or protiptyline were infused intravenously into anaesthetized rabbits. The concentrations of the antidepressants 5 minutes after the termination of the infusion were measured by gas chromatography in the plasma, heart ventricles, and femoral muscle. On average, the concentrations in the heart were 40 to 200 times higher than those measured in plasma, the concentration of protriptyline being highest. The heart/plasma concentration ratios were higher for protriptyline and amitriptyline than for nortriptyline and doxepin. The toxicity of the antidepressants correlated neither to their heart concentrations nor to their heart/plasma concentration ratios. The different acute cardiotoxicity of tricyclic antidepressants cannot be explained by their different concentrations in the plasma or in the heart muscle only, but seem to have different toxic potencies. 14 references. (Author abstract modified)

000459 Engel, J.; Lundborg, P. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Reduced turnover in mesolimbic dopamine neurons in 4-week-old offspring of nursing mothers treated with penfluridol.** Brain Research (Amsterdam). 110(2):407-412, 1976.

The effect of alpha-methyl-p-tyrosine, an inhibitor of tyrosine hydroxylase, on the disappearance of dopamine (DA) and noradrenaline (NA) in the brain of 28-day-old offspring of rats treated with penfluridol or glucose during the first postnatal week was studied in order to determine the nature of the biochemical brain-damage produced in infants of nursing mothers receiving penfluridol. No difference between penfluridol treated and glucose treated offspring is observed in the disappearance of NA from the hemispheres of the limbic system. A pronounced retardation in the rate of disappearance of DA from the limbic system, but not from the striatum, occurs in the penfluridol treated offspring. It is suggested that there is a reduced nerve impulse activity in the mesolimbic DA neurons in the 4-week-old offspring of nursing mothers treated with penfluridol. It is further suggested that this dysfunction is probably responsible for the impaired acquisition of conditioned avoidance behavior observed in these animals. 14 references.

000460 Guilleminault, Christian; Eldridge, Frederic L.; Phillips, James R.; Dement, William C. Sleep Disorder Clinic and Laboratory, Stanford University School of Medicine, Stanford, CA 94305 **Two occult causes of insomnia and their therapeutic problems.** Archives of General Psychiatry. 33(10):1241-1245, 1976.

Studies on two specific syndromes, sleep apnea and abnormal swallowing reflex syndrome which may produce insomnia, and in which hypnotics and depressants are potentially harmful, are presented. The symtoms and drug reactions of patients with both syndomes are described, and it is concluded that central nervous system depressants should be cautiously prescribed for patients with such syndromes. 9 references. (Author abstract modified)

000461 Hughes, J. A.; Rosenthal, E.; Sparber, S. B. Department of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **Time dependent effects produced in chicks after prenatal injection of methylmercury.** Pharmacology Biochemistry and Behavior. 4(5):507-513, 1976.

Experiments were conducted using chick embryos to determine: 1) whether a behavioral effect of early exposure to methylmercury is time related; 2) which period(s) of embryogenesis is (are) most important; 3) how much methylmercury reaches the embryo; and 4) when maximal levels of the alkylmercurial are attained in the embryo brain relative to embryolethal effects and behavioral effects. Methylmercury dicyandiamide (0.05mg/kg egg to 10mg/kg egg) injected into the yolk sac of fertilized chicken eggs prior to incubation produces a dose related decrease in the percentage of chicks hatched. Injection of 0.5mg/kg egg on day 0, day 7, or day 14 of incubation reduces the number of chicks hatched to 90%, 68% and 75% of controls respectively. Injection of 5.0mg/kg egg on day 0, day 7, or day 14 of incubation reduces the number of chicks hatched to 63%, 13% and 18% of controls, respectively. Chicks hatched from eggs injected on day 7 or day 14 do not differ from controls in a detour learning situation but chicks hatched from eggs injected on day 0 exhibit longer cumulative detour response latencies than do controls. Administration of 14C-methylmercury reveals maximal brain radiolakel in embryos injected on day 0 to be 10% of that in eggs injected on day 7 and twice that in eggs injected on day 14. It is tentative-

ly concluded that a period of maximal sensitivity to the behvioral effects of mercury exists prior to day 7 and that the mechanism producing embryolithality differs from the mechanisms producing the functional deficits. 28 references. (Author abstract modified)

000462 Lehmann, Horst. Abteilung fur Experimentelle Pathologie, Dr. Karl Thomae GmbH, 7950 Biberach an der Riss, West Germany **/Teratological studies of rabbits and rats treated with the morphine derivative codeine./** Teratologische Untersuchungen an Kaninchen und Ratten mit dem Morphinabkommling Codein. Arzneimittel-Forschung (Aulendorf). 26(4):551-554, 1976.

Codeine was administered to rabbits and rats to study its teratological effect. Codeine was administered to rabbits and rats during the organogenetic phase (days 6 to 18 and 6 to 15 resp.)in oral doses of 5mg/kg, 12.5mg/kg and 30mg/kg and 10.35 and 120mg/kg, respectively. The tests in rabbits yielded no indication of a teratogenic or embryolethal action of the substance under investigation. Even in the experiments with rats no teratogenic effect was realized. The highest dose of 120mg/kg, which was in the toxic range for the mother animal, led to an increased mortality of rat embryos around the time of implantation. These experiments indicate no increased risk during pregnancy due to codeine. 11 references. (Author abstract modified)

000463 Marshall, John F.; Leviton, Deborah; Stricker, Edward M. Psychobiology Program, Department of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Activation-induced restoration of sensorimotor functions in rats with dopamine-depleting brain lesions.** Journal of Comparative and Physiological Psychology. 90(6):536-546, 1976.

Bilateral electrolytic lesions of the lateral hypothalamus or intraventricular 6-hydroxydopamine injections produced substantial depletions of striatal dopamine in rats. All animals with brain damage showed marked sensorimotor impairments. However, they began to move and respond appropriately to environmental stimuli when placed in a sink of water, in a shallow ice bath, or among a colony of cats or rats. A reversal of the sensorimotor dysfunctions was still apparent shortly after the animals were removed from each activating situation. However, the therapeutic effects dissipated rapidly, and by 4 hrs after an exposure the rats responded as poorly as they had prior to activation. These findings are strikingly similar to the "paradoxical kinesia" seen in parkinsonism, a clinical disorder attributed to degeneration of central dopamine containing neurons. Collectively, they suggest the importance of activation in maintaining responsiveness to sensory stimuli in rats following dopamine depleting brain lesions. 36 references. (Author abstract)

000464 Ruckebusch, Yves; Gaujoux, Monique; Eghbali, Behrokh. Laboratoire de Physiologie et Pharmacodynamie, Ecole Nationale Veterinaire, F-31076 Toulouse Cedex, France **Placental transfer of central nervous system depressants in sheep.** European Journal of Pharmacology (Amsterdam). 37(1):193-196, 1976.

Drugs used during birth labor were administered to conscious sheep near term to determine the effects on fetal brain reactivity and therefore placental transfer and presence in the fetal brain. Continuous monitoring of the fetal electrocorticogram (ECG), eye movements and heartrate show rapid placental transfer from the mother to the fetus of phenothiazine derivatives (acepromazine maleate), short acting barbiturates (thiopental sodium) and narcotic analgesics (meperidine). Acepromazine and thiopental partially disrupt the fetal sleep cycle by synchronization of the ECG for 1-2 hr but increase the heartrate for 2-3 hr. The effects of meperidine are similar but last only 5-10 min for the ECG and less than 0.5hour for the heartrate. 10 references. (Author abstract modified)

000465 Takeichi, Masashi. Dept. of Neuropsychiatry, Kyushu University Medical School, Kyushu, Japan **Effect of L-Dopa administration to fine structures of the brain, heart, and kidney in rats, with special reference to the appearance of microvascular thrombosis and its pathological significance.** Psychiatria et Neurologia Japonica (Tokyo). 77(7):539, 1975.

The long-term effects of L-Dopa administration were tested by orally feeding rats 100-200mg/kg of body weight for a period of three months. Monthly autopsies on some of the rats showed that in the brains, heart, and kidneys, microvascular nest-like configurations appeared. Due to the coagulation of red blood cells, thrombosis appeared. Examination under an electron microscope showed that there were possibly two types of changes occurring. One was a change in the innerwall of the capillaries -- some kind of thrombosis producing substance was present. The other change was noted in the brain nerve cells, the heart muscle cells, and the kidney cells. There was an abnormailty of their mitochrondria. The longer L-Dopa was administered to the rats, the more pronounced these changes became. Thus possible damage to these organs must be considered when administering L-Dopa over a long period of time.

000466 Yih, T. D.; Van Rossum, J. M. Department of Pharmacology, University of Nijmegen, Nijmegen, The Netherlands **Peculiar pharmacokinetics of brallobarbital as a source of complications in Vesparax intoxication.** Xenobiotica (London). 6(6):355-362, 1976.

Pharmacokinetics of brallobarbital are described as a source of complications in intoxication by Vesparax, a potent barbiturate-hydroxyzine combination frequently used in suicide attempts. The rate of elimination of brallobarbital, a component of Vesparax, was shown to depend on route of administration. The half-life following oral administration in rats is considerably longer than after intravenous injection, corresponding with longer sleeping times. The half-life of brallobarbital administered intravenously was increased by administration of its metabolites, suggesting that a metabolite formed especially after oral administration is responsible for retarded elimination of brallobarbital. The presence of the other components of Vesparax, secobarbital and hydroxyzine, also increased the half-life of brallobarbital as tested in rats. It is concluded that brallobarbital, rather than other components of Vesparax, is primarily responsible for complications occuring in Vesparax intoxication. 12 references. (Journal abstract modified)

06 METHODS DEVELOPMENT

000467 Carolei, A.; Margotta, V.; Palladini, G. Clinica delle Malattie Nervose e Mentali, University of Rome, 30 viale dell'Universita, I-00185 Rome, Italy **Proposal of a new model with dopaminergic-cholinergic interactions for neuropharmacological investigations.** Neuropsychobiology (Basel). 1(6):355-364, 1975.

An investigation of organisms located at lower phylogenetic levels as simpler models for neuropharmacological investigations is reported, describing the planaria Dugesia gonocephala. Drugs studied in the proposed species included L-dopa, beserazide, dehydroemetine hydrochloride, d-amphetamine, apomorphine sulphate, atropine sulphate, physostigmine sal-

icylate, piribedil, haloperidol, reserpine, clonidine, biperiden, 2-BRdalpha-ergocryptine, melanocyte stimulating hormone release inhibiting factor, and thyrotropin releasing hormone. The motor system of Dugesia gonocephala shows a striking similarity with the extrapyramidal system of high vertebrates and of man with the evidence of correlations between dopaminergic and cholinergic neurons. The utilization of this model seems to be especially useful in testing drugs which presumably act on dopaminergic or cholinergic transmission. In this model, the quantification of animal behavior seems considerably easier when compared with the difficulties met in other animal models commonly employed. Besides, it might be anticipated that this model, if correctly used, can display interesting perspectives also in neuroendocrinological investigations. 39 references. (Author abstract modified)

000468 Da Prada, Mose; Zurcher, Gerhard. F. Hoffmann-La Roche and Company, Ltd., Pharmaceutical Research Department, CH-4002 Basle, Switzerland **Simultaneous radioenzymatic determination of plasma and tissue adrenaline, noradrealine and dopamine within the femtomole range.** Life Sciences (Oxford). 19(8):1161-1174, 1976.

A newly developed radiometric/enzymatic assay for measuring simultaneously femtomole quantities of adrenaline, noradrenaline, and dopamine is described. The three catecholamines are first converted to their 0-methylated analogues by catechol-0-methyltransferase in the presence of S-adenosyl-methionine-3H and thereafter extracted following addition of sodium tetraphenylborate. This extraction, together with an improved quick chromatographic separation and the oxidation of the adrenaline and noradrenaline derivatives to vanillin, yields an extremely high sensitivity and specificity to the method. The present assay allows the determination of adrenaline, noradrenaline, and dopamine in tissue samples with a protein content of 100 micrograms or less and in plasma volumes of 20 to 100 microliters. The amine content of 40 to 50 samples can be determined in 2 days by one person. Due to the high sensitivity achieved, this method promises to be a valid alternative to the gas chromatography/mass spectrometry technique. 20 references. (Journal abstract)

000469 Davidson, Arnold B.; Weidley, Edwin. Department of Pharmacology, Hoffmann La Roche Inc., Nutley, NJ 07110 **Differential effects of neuroleptic and other psychotropic agents on acquisition of avoidance in rats.** Life Sciences (Oxford). 18(11):1279-1284, 1976.

An avoidance acuisition procedure, which is specifically sensitive to the effects of clinically effective antipsychotic (neuroleptic) agents and predictive of their clinical potency, is presented. The method distinguishes between such compounds and other classes of psychotropic agents. It utilizes experimentally naive rats, thereby obviating the need for maintaining colonies of trained animals, requires no training by the experimenter, and is rapid, requiring only a single, 50 min test session. 15 references. (Author abstract)

000470 Ervik, Magnar. Department of Analytical Chemistry and Biochemistry, AB Hassle, Fack, S-431 20 Molndal, Sweden **Quantitative determination of metoprolol in plasma and urine by gas chromatography.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):136-144, 1975.

A procedure for the gas chromatographic determination of the beta-receptor blocking agent metoprolol at therapeutic levels in plasma and urine is described. Metoprolol is made electron capture sensitive by a derivatization reaction with trifluoroacetic anhydride. The method permits determination of concentrations of metoprolol down to about 5ng/g of sample with a standard deviation of 0.7ng. Automation of the gas chromatographic procedure gives a capacity of 24 samples a day. 6 references. (Author abstract)

000471 Koga, Yoshihiko. Pharmaceuticals Division, Sumitomo Chemical Co., Ltd. 4-2-1, Takatsukasa, Takarazuka, Hyogo 665, Japan **Induction of physical dependence in rats by short interval medication.** Psychopharmacology (Berlin). 50(2):153-157, 1976.

A method utilizing an intermittent infusion system that gives hourly injections of a drug to rats was used to study the development of physical dependence to morphine, codeine, pentazocine and ID-1229, a new benzomorphan analgesic. Physical dependence on morphine and codeine developed rapidly and was detectable with low daily maintenance doses. Physical dependence on pentazocine also developed but daily maintenance doses required to produce physical dependence were much higher than with morphine or codeine. Cross-dependence between morphine and pentazocine was demonstrated; pentazocine suppressed the abstinence signs in rats weakly dependent on morphine and morphine suppressed those of pentazocine dependent animals. ID-1229 did not produce dependence in this test and did not suppress the abstinence signs of morphine dependent animals or pentazocine dependent animals. 7 references. (Author abstract modified)

000472 Nozaki, Masako. Addiction Research Center, National Institute on Drug Abuse, P.O. Box 12390, Lexington, KY 40511 **Assessment of morphine-type physical dependence liability: a screening method using the rat.** Psychopharmacology (Berlin). 47(3):225-235, 1976.

The effects of 24 centrally acting drugs on bodyweight changes during 8 hour periods in the daytime were studied in the rat in attempts to relate those effects with morphine type physical liability. Repeated administration of drugs which have morphine type physical dependence liability altered the prevailing pattern of continuous bodyweight decrease during the observation period in control animals to an initial increase and subsequent decrease. Withdrawal of these drugs following chronic drug treatment caused a precipitous loss of body weight which was further enhanced by administration of naloxone. In chronically morphine treated animals, substitution for morphine with a single dose of test drug caused an increase in bodyweight or attenuated the loss of bodyweight due to morphine witdrawal when the test drug has physical dependence liability. Drugs may be classified according to their effects on bodyweight changes into several groups, each with different physical dependence liability. It is concluded that physical dependence liability of centrally acting drugs can be predicted by their effects on the pattern of daily bodyweight changes of the rat. 49 references. (Author abstract modified)

000473 Pollock, B.; Bock, P. R.; Fuchs, A. M.; Lohaus, R. Department of Pharmacology, Dr. Thiemann GmbH, 4670 Luenen, West Germany **Visually evoked potentials in cortical and subcortical brain structures of conscious rabbits with chronically implanted electrodes: standardized normal values and the influence of some psychopharmacological agents on them.** Arzneimittel-Forschung (Aulendorf). 26(3):327-334, 1976.

The effectiveness of using visually evoked potentials (EP) as a means of investigating and classifying newly developed psychotropic drugs was studied. By means of a modified and simplified surgical and implantation technique, standardized values for EPs in 26 conscious rabbits from 7 brain structures (caudate nucleus, posterior hypothalamus, mesencephalic

reticular formation, intralaminar thalamic nuclei, amygdala, dorsal hippocampus and visual cortex) were obtained. The importance of a careful selection of the animal material, constant test conditions and the selection of test parameters for the assessment of psychotropic drugs is emphasized and discussed. The effects of haloperidol and amytriptyline on latencies and amplitudes of the individual parameters of EPs are described as an example of the specific influence on EPs in the above named brain structures. Thus it may be established that amitriptyline and haloperidol as classic representatives of antidepressants and neuroleptics have a varying and sometimes contrasting influence on certain EP components. Satisfactory statements of fundamental neurophysiological mechanisms of action cannot be made on the basis of this method. It may be assumed that the technique described can be of great assistance in the classification and investigation of newly developed substances. 44 references. (Journal abstract modified)

000474 Seeman, P.; Lee, T.; Chau-Wong, M.; Wong, K. Department of Pharmacology, University of Toronto, Toronto, Canada M55 LA8 **Antipsychotic drug doses and neuroleptic/dopamine receptors.** Nature (London). 261(5562):717-719, 1976.

Antipsychotic drugs of various chemical structures are tested for their effects on the stereospecific binding of haloperidol. Binding of 3H-haloperidol was done on calf caudate homogenates, and binding of 3H-dopamine was done using rat caudate. The stereospecific component of binding was defined as that amount of 3H-haloperidol or 3H-dopamine bound in the presence of (-)-butaclamol (inactive neuroleptic) minus that bound in the presence of (+)-butaclamol (active neuroleptic). The antipsychotic drugs tested were: promazine, chlorpromazine, trazodone, clozapine, thioridazine, molindone, prochlorperazine, moperone, trifluperazine, thiothixene, droperidol, fluphenazine, pimozide, trifluperidol, benperidol and spiroperidol. The results indicate that there is a good correlation between the antipsychotic potencies needed for controlling schizophrenia and the IC50 values (concentrations producing 50% blockade of haloperidol binding). This neuroleptic receptor assay can then be used to screen potentially antipsychotic drugs. 18 references.

000475 Valzelli, L.; Bernasconi, S. Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62-20157 Milan, Italy **Psychoactive drug effect on behavioural changes induced by prolonged socio-environmental deprivation in rats.** Psychological Medicine (London). 6(2):271-276, 1976.

The theory that animal emotionality may alter the outcome of psychoactive drug administration is tested. Male Wistar rats are isolated for several weeks. Such prolonged socioenvironmental deprivation produces three typical behaviors when a naive normal rat is introduced: muricide behavior (30%); friendly behavior (25%); indifferent behavior (45%). These changes in normal behavior patterns are assumed to reflect a series of different emotional changes. Forty drugs (antipsychotic, antianxiety, antidepressant, and hallucinogenic) and electroshock are administered, and it is shown that they can exert a different effect in relation to the different kinds of animal behavior. It is suggested that investigations of psychoactive drug properties would be more fruitful if performed in experimental animals exibiting behavioral alterations than in normal laboratory animals. 36 references.

000476 Van Dorsser, W. no address **/Evaluation techniques in the study of tricyclic antidepressants./** Techniques d'evaluation des antidepressifs tricycliques. Feuillets Psychiatriques de Liege (Liege). 8(4):434-446, 1975.

Various techniques of laboratory evaluation of the antidepressant activity of a substance are reviewed with emphasis on behavioral studies and other animal studies and on studies treating the interaction with biogenic amines on the peripheral and central nervous system. Research experiments described include: inhibition of the effects of reserpine; the dopa response potentiation; potentiation of the effects of amphetamine; antagonism of catalepsy induced by neuroleptics; antagonism of the effects of central cholinergics; potentiation of the toxicity of yohimbine; potentiation of yohimbine and 5-HTP; inhibition of interspecific aggressivity; and interaction of antidepressants with the biogenic amines. It is concluded that assessment of the inhibition of the uptake of amines in nerve endings may be considered the most interesting test of antidepressant therapeutic activity.

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

000477 Amphoux, G. Service de Neuro-Psychiatrie, C. H. R., 5, rue Hoche, F-3400 Nimes, France /**A new medication of the antidepressant group: Vagran 50 (propizepine hydrochloride).**/ Un nouveau medicament du groupe des antidepresseurs: Vagran 50 (chlorhydrate de propizepine). Psychologie Medicale (Paris). 8(2):305-310, 1976.

Propizepine, a drug related to the tricyclic antidepressants, was studied in 30 patients with neurotic or reactive depression who were hospitalized on an open service. A self-evaluation scale and a simplified Hamilton scale were used for ratings. The dosage of propizepine was 200-300mg/day, and the mean length of treatment was 1 month, with treatment rarely exceeding 1 1/2 months. Tricyclic and MAOI antidepressants were not given concomitantly with propizepine, nor was lithium, but some patients received tranquilizers and/or hypnotics. No side-effects were noted. One patient ingested half a bottle of propizepine after discharge, and recovered the next day without hospitalization. The patients ranged in age from There were 21 women and 9 men. Of the 30 patients, 10 showed good results, 10 showed slight results, and 10 showed no results. Neither of the 2 patients with endogenous depression responded, and 3 of the 5 involutional depressives did not respond. Results were best with the 16 reactive and neurotic depressives, 6 patients showing good improvement and 7 showing slight improvement. Propizepine seemed to have both an antidepressant and an antianxiety effect.

000478 Angrist, B; Rotrosen, J.; Aronson, M.; Gershon, S. Department of Psychiatry, Neuropsychopharmacology Research Unit, New York University Medical Center, New York, NY 10003 **A morphanthridine derivative in schizophrenic patients -- lack of extrapyramidal symptoms.** Current Therapeutic Research. 20(1):94-98, 1976.

A study was understaken to obtain dose tolerance data and a crude initial index of neuroleptic efficacy for EX 11-582A, a morphanthridine derivative. Ten hospitalized schizophrenic patients were treated with a mean maximum daily dose of 158mg; the mean duration of treatment was 20 days. At termination, four patients showed complete remission of symptoms and could be discharged. Two patients were judged somewhat worse at termination and two showed definite deterioration. Extrapyramidal symptoms were not noted but anticholinergic side effects (abdominal distress, nausea and vomiting, dry mouth and blurred vision) occurred in four patients. 1 reference. (Author abstract modified)

000479 Aquino, J. P. Service de Medicine Interne, Hopital d'Ivry, Ivry, France /**Trimethozine in a geriatric milieu.**/ La trimetozine en milieu geriatrique. Revue de Gerontologie d'Expression Francaise (Paris). No. 3:51-53, 1975.

Trimethozine, a trimethoxybenzoic acid derivative corresponding to the trimethoxy-3, 4, 5-benzoyl-4-morpholine group, was studied in 21 geriatric patients presenting with anxiety. The 8 men and 13 women had mean ages of 73 and 80 years, respectively. Dosage ranged from 600 to 1800mg/day, with a mean of 1200mg/day. Other psychotropic drugs were not given. Patients were rated on 16 items before treatment and on the 7th and 21st days of treatment. Improvement occurred on 14 of the 16 test items, with greatest improvement observed in expressed anxiety, tension, depressive tone, and sleep problems. Tolerance was excellent, with only 2 cases of daytime sedation noted.

000480 Arnold, Elisabeth. Dept. of Biology, DUMEX, 37, Prags Boulevard, DK-2300 Copenhagen S, Denmark **A simple method for determining diazepam and its major metabolites in biological fluids: application in bioavailability studies.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(4):335-352, 1975.

A simple gas chromatographic analytical method for determining diazepam and its major metabolites in the blood, urine, and muscle homogenate is described. Its applicability is illustrated by bioavailability studies, on man and on animals. The human studies revealed equivalence between two marketed brands of diazepam tablets and a slight difference between two brands of suppositories. The animal experiments showed agreement of in vivo properties of two different formulations of a diazepam injection fluid. The use of diazepam as a tranquilizer for humans is stressed. 18 references. (Author abstract modified)

000481 Bedoret, J. M.; Meaux, J.-P. 28-30, rue de Soubise, Dunkerque, France F-59140 Dunkerque, France /**Anti-anxiety action of Tranxene 50 mg.**/ L'action anxiolytique du Tranxene 50mg. Psychologie Medicale (Paris). 8(5):791-795, 1976.

Effects of the 50mg dose of Tranxene were studied in 39 outpatients, of whom 19 were male and 20 female. Diagnoses were neurosis in 29, psychosis in 5, and object loss manifestations in 5. The 50mg dose was prescribed in the evening, with the 5mg and 10mg doses given during the day. The average daily dose was 70mg. The higher doses were given to psychotic patients and the severely obsessional patients. Some patients received antidepressants in addition to Tranxene. A decrease in vigilance was noted in five patients. Results were very good in 14 patients, good in 1three, mediocre in 9, and no improvement in three. The 3 patients failing to respond were obsessional (1) or psychotic (2). The antianxiety effect was obtained during the first few days. In patients responding favorably it was possible to reduce the dose after 15 days. Patients with anxiety neurosis responded better than patients with obsessional neurosis who, in turn, responded better than psychotics. 19 references.

000482 Ben-Bassat, Avraham A.; Lavie, David; Edery, Habib; Porath, Gila. Department of Organic Chemistry, Weizmann Institute of Science, Rehovot, Israel **Quaternary pilocarpine derivatives as potential acetylcholine antagonists. 2. Alterations in the lactone and imidazole moieties.** Journal of Medicinal Chemistry. 19(7):928-933, 1976.

In investigating the chemical behavior of pilocarpine, as well as factors determining its pharmacological activity, systematic and specific structural changes were performed involving the lactone and imidazole moieties. Series of model compounds with cyclic or open chain structures and a variety of N-3 bonded chains obtained from previously prepared anticholinergic derivatives of pilocarpine were synthesized. The changes included N-3 chains of different lengths with an acetycholine like structure, the introduction of nucleophilic groups such as ketoxime, hydroxamic, or both at the side chain, or following hydroxylaminolysis of the lactone, respectively. Specific structural alterations could be obtained by reacting with free hydroxylamine under carefully controlled conditions, and the

existence of synisomers and antiisomers was disclosed in certain cases. The new compounds displayed some antidotal activity. 23 references. (Author abstract modified)

000483 Bogdanowicz, Elzbieta; Bojdecki, Krzysztof. II. Klinika Psychiatryczna Instytutu Psychoneurologicznego, Al. Sobieskiego 1/9, 02-957 Warsaw, Poland **/Methodlogical problems in clinical evaluation of psychotropic drugs./** Problemy metodologiczne klinicznej oceny lekow psychotropowych. Psychiatria Polska (Warszawa). 10(1):3-13, 1976.

Problems in the evaluation of psychotropic drugs include the methodological aspects of: criteria for treatment; the need for a worldwide scale for comparing results; safety problems; ethical and legal issues. Based on a WHO report, 2 distinct phases of the use of a drug before it is made generally available are suggested: an exploratory stage, wherein the biochemical properties of the drug, the nature of its effect, maximum dosage and tolerance, and its potential use in particular diseases are analyzed; and a stage of controlled clinical treatment of patients, wherein its efficiency, precise dosage, possible use in conjunction with other drugs, and the criteria for patient selection are investigated. These problems are discussed in relation to the specific diseases of manic-depression, schizophrenia, and various phobias. 42 references.

000484 Bornstein, S.; Tournoux, C.; Kamoun, A.; Labet, R. Hopital Psychiatrique de la Maison-Blanche, 3, avenue J. Jaures, F-92200 Neuilly-sur-Marne, France **/Activity of 1694 in the treatment of neurotic states, whether structured or not, having psychasthenic, anxious-phobic and depressive expression./** Activite du 1694 dans le traitement des etats nevrotiques structures ou non, a expression psychasthenique, anxio-phobique et depressive. Semaine des Hopitaux (Paris). 52(1):15-17, 1976.

The drug 1694 (Survector 100), a tricyclic drug having a heptanoic acid side chain, was studied to determine its psychotropic properties. Its pharmacological properties are briefly summarized. The drug was given to 100 adults of both sexes ranging in age from 16 to 75 years old. The dose was 100-200mg and the treatment ranged in duration from several days to 19 months. The patients suffered from a variety of neurotic and depressive symptoms. A global evaluation was used and the results were excellent in 30 subjects, good in 28 subjects, fair in 15 subjects, no change in 21 subjects and aggravation or drug intolerance in 6 subjects.

000485 Bukowczyk, Adam; Wasik, August; Horodnicki, Jan; Plotczyk, Jadwiga. Klinika Psychiatryczna AM, ul. Kraszewskiego 25, 50-229 Wroclaw, Poland **/Intravenous administration of Maprotylin in depression./** Dozylne stosowanie maprotyliny w stanach depresyjnych. Psychiatria Polska (Warsawa). 10(1):89-91, 1976.

Fifteen females, 29 to 60 years of age, in depressive states (9 endogenous depression and 6 involutional depression), 12 of whom had suicidal tendencies, were treated with an average of 175mg Maprotylin i.v. for an average period of 12 days. A distinct improvement was observed in three patients and a slight improvement was noted in five patients. Tolerance to the drug was high and physiological side-effects were minimal. It is concluded from this study that intravenous Maprotylin is less successful than other methods of treating depression.

000486 Carranza, J.; Saldana, H.; Ramirez, A. Baylor College Medicine, VA Hospital, 2002 Holcombe, Houston, TX 77211 **Double-blind evaluation of AHR-1118 and amitriptyline in depressed patients.** Current Therapeutic Research. 20(4):552-556, 1976.

Results of a double-blind study testing the efficacy of 3(diphenylmethylene)-1-ethyl-pyrrolidine HCl (AHR-1118) as an antidepressant against amitriptyline with 30 depressed patients are summarized. No overall diffference was found between the therapeutic effects of the two substances. Slight differences suggested that the antidepressant effect of AHR-1118 appears earlier. The appearance of insomnia and the effectiveness of AHR-1118 in treating motor retardation suggest that it belongs to the group of antidepressants with more thymoleptic than sedative effect, similar to imipramine. 4 references. (Journal abstract modified)

000487 Castaigns, G.; Chartres, J. P. Centre Hospitalier specialise Charles-Perrens, 121, rue de la Bechdae, F-33000 Bordeaux, France **/Clinical study of Lin 1418 (sultopride)./** Experimentation clinique du Lin 1418 (sultopride). Psychologie Medicale (Paris). 8(1):113-120, 1976.

Sultopride, a substituted benzamide, was studied in 54 patients over an 8 month period. Most of the patients were hospitalized and chronic. The 33 females and 21 males ranged in age from 19 years old to 73 years old. The drug was given orally to 39 patients and i.m. to 14. The dosage ranged from 400-2400mg/day, and the duration of treatment ranged from 15 days to 7 months. Patients also received other tranquilizers, sedatives, and hypnotics. Diagnoses included acute psychoses (delirium, mania), agitated states in alcoholics, behavior and character disorders (epilepsy, psychopathic personality, mental retardation, presenile and senile dementia), and chronic psychosis (schizophrenia, paranoid, chronic hallucinatory psychosis). Excellent results were obtained in the acute psychotics, with irregular results being obtained for other diagnoses. Side-effects occurred in 37 patients and included hypotension, extrapyramidal symptoms (in 29), amenorrhea, galactorrhea, and an anxiety-depressive syndrome (in 8). 26 references.

000488 Corsini, G. U.; Del Zompo, M.; Cianchetti, C.; Mangoni, A.; Gessa, G. L. Institute of Nervous and Mental Diseases, University of Cagliari, Cagliari, Italy **Therapeutical efficacy of a combination of apomorphine with sulpiride or metoclopramide in Parkinsonism.** Psychopharmacology (Berlin). 47(2):169-173, 1976.

In healthy volunteers the emetic effect of apomorphine (5-10mg, i.m.), a potent direct stimulant of dopamine receptors, was prevented by haloperidol (2mg), metoclopramide (10mg) and sulpiride (100mg), injected intramuscularly. In Parkinsonian patients, apomorphine (1mg) given alone ameliorated the neurological symptoms (30% improvement in the disability score), but the improvement was accompanied by nausea, vomiting, sedation or sleepiness. Haloperidol prevented not only the emetic effect of apomorphine, but also its therapeutic efficacy in Parkinsonism. Indeed, the disability score was worsened by the drug combination in some patients. Moreover, after haloperidol, apomorphine produced deep sedation and sleep. By contrast, in Parkinsonian patients pretreated with metoclopramide or sulpiride, apomorphine markedly diminished tremor and rigidity and failed to produce nausea, vomiting and sleepiness. 22 references. (Author abstract modified)

000489 d'Elia, Giacomo. Psykiatriska Kliniken I, Sahlgrenska Sjukhuset, 413 45 Goteborg, Sweden **/Patients' reactions to clinical drug testing./** Hur upplever patienter en klinisk lakemedelsprovning? Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(7):587-596, 1975.

Patients' reactions to clinical drug testing are studied and a double-blind crossover comparison with the antidepressant Lofepramine (LEO 640) was made. Imipramine was used as reference drug. The 32 participating patients were all informed about the trial. EKG, plasma and plasma concentrations were taken at fixed hours by the five doctors involved in the experiment. The treatment's therapeutic effect was measured by Cronholm-Ottosson's scale. Six to 12 months after the trial, two questionnaires, one consisting of ten questions and one of 40 questions, were presented to the patients. About 2/3 of the patients were neutral or positive to the trial. Correlation coefficients, measured with Spearman's method, showed that an accepting attitude to the drug combined with a positive attitude to the drug's therapeutic effect and a somatic attitude, correlated with a positive result of the treatment. 23 references.

000490 Fabre, Louis F.; McLendon, David M.; Harris, Robert T. Fabre Clinic, 5503 Crawford Street, Houston, TX 77004 **Preference studies of triazolam with standard hypnotics in out-patients with insomnia.** Journal of International Medical Research (Northampton). 4(4):247-254, 1976.

One hundred and four patients suffering from insomnia took part in four different two night double-blind crossover trials of triazolam. In three separate studies, triazolam 0.5mg was compared to placebo, flurazepan 30mg and chloral hydrate 500mg. Triazolam 0.5mg was found to be preferred and to be superior to placebo, flurazepan and chloral hydrate in the treatment of insomnia. Analysis of sleep questionnaire data showed triazolam to be superior to the other treatments on the following: How much did the medication help you sleep, onset of sleep, duration of sleep and number of awkenings. Additionally, triazolam was superior to chloral hydrate on the feeling in the morning parameter. In another comparison of triazolan 0.25mg to flurazepan 15mg, triazolan was not significantly better than flurazepan on any of the efficacy parameters except that the patients felt more alert the morning following flurazepan. On all efficacy endpoints, trends for all parameters favored triazolan 0.25mg over flurazepan 15mg. Untoward side-effects in these four studies were minimal. 8 references. (Journal abstract)

000491 Gentil, V.; McCurdy, R. L.; Alevizos, B.; Lader, M. H. Institute of Psychiatry, Clinical Psychopharmacology, Section, De Crespigny Park, London SE5 8AF, England **The effects of adrenaline injections on human platelet monoamine oxidase and related measures.** Psychopharmacology (Berlin). 50(2):187-192, 1976.

A double-blind, placebo controlled crossover study in 10 normal subjects assessed the effects of subcutaneously administered adrenaline on platelet monoamine oxidase (MAO) activity. MAO activity towards benzylamine was significantly increased by adrenaline. Nonsignificant increases were noted in the deamination of tyramine, the deamination of tryptamine, platelet counts, cortisol concentrations and metaraminol uptake. Increases in MAO activity were also noted early in the experimental sessions suggesting that other experimental variables such as venepuncture may affect platelet MAO activity. Possible mechanisms for this adrenaline effect are discussed and it is suggested that variables such as arousal and emotional stress must be taken into account when interpreting clinical data on platelet MAO in psychiatric patients. 20 references. (Author abstract modified)

000492 Gianfranceschi, G.; Bellini, M. no address **Psychosomatic approach to ophtalmologic patients treated with trazodon.** Medicina Psicosomatica (Roma). 20(4):394, 1975.

A report discussing the psychosomatic approach to ophtalmologic patients treated with trazodon was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Primary glaucoma patients admitted to an ophthalmologic ward and treated with Trazodon were observed. At the beginning of the treatment and at later intervals clinical oculistic parameters and quantified psychological parameters were observed to verify whether the drug can induce clinical ocular alterations, especially in ocular tension, and whether the drug had psychotropic action in these patients. (Author abstract modified)

000493 Goldman, Douglas. 179 East McMillan Street, Cincinnati, OH 45219 **Treatment of phenothiazine-induced dyskinesia.** Psychopharmacology (Berlin). 47(3):271-272, 1976.

The possibility that a serotonin antagonist might be effective in relieving dyskinesia resulting from phenothiazine administration was investigated in three patients. The patients had dyskinesia with choreiform and athetoid movements but not dystonia. Cyproheptadine, an antihistamine which produces strong serotonin antagonism was administered. Cyproheptadine was definitely effective in relieving the symptoms over an extended period of time. Further controlled studies are required. 3 references. (Author abstract modified)

000494 Guran, Ph. Service de Pediatrie, Centre Hospitalier, 1, rue Richaud, F-78000 Versailles, France /**Study in a pediatric milieu of an antianxiety drug: clobazam.**/ Etude en milieu pediatrique d'un anxiolytique: le clobazam. Annales de Pediatrie (Paris). 23(6-7):489-491, 1976.

Cloazam (Urbanyl), a new benzodiazepine derivative was studied in 35 pediatric outpatients ranging in age from 9 months to 13 years. The average age was 7 years old. The patients suffered from anxiety, which was manifested by insomnia, abdominal pains, instability and aggressiveness. The daily dose was 0.5mg/kg, with half given in the morning and the other half in the evening, over a period of 4 weeks. No other drugs were given concomitantly. Patients were rated on a scale from zero to four at the beginning and end of treatment. Good results were obtained in 17 of the 18 patients with insomnia, 12 of 14 patients with aggressiveness and 21 of 23 patients with general anxious behavior. Tolerance was excellent, except for 1 patient who developed somnolence.

000495 Heller, B.; Fischer, E.; Martin, R. Lab. de Psicofarm. y Neuropsiqu. Exper. de la Fac. de Med., Univ. Nacional de Buenos Aires, Barracas 375, Buenos Aires, Argentina **Therapeutic action of D-phenylalanine in Parkinson's disease.** Arzneimittel-Forschung (Aulendorf). 26(4):577-579, 1976.

An open field trial of D-phenylalanine was made in 15 patients with Parkinson's disease of 6 months' to 13 years' duration. All medication was suspended 10 days before the trial, and the patients received only 200mg-500mg D-phenylalanine daily, divided into 2 doses, for 4 weeks. Positive results were highly significant in relation to rigidity, walking disabilities, speech difficulties, and mental depression, but no significant therapeutic results were obtained in regard to tremor. The therapeutic action on the total development of the disease may be considered highly significant. The results suggest a special cholinergic origin of tremor in Parkinson's disease, and in these cases a combination of the amino acid with anticholinergic agents should be tried. 20 references.

000496 Heltberg, Jon; Kirk, Lars; Moller, Svend Erik. Sct. Hans Hospital, Afd. D, DK-4000 Roskilde, Denmark /**Four methods of treating senile melancholy with tryptophan and lithi-**

um./ Fire tilfaelde af behandlingsresistent senil melankoli bedret under behandling med tryptofan + litium. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):463-464, 1975.

The effect of the combination tryptophan/lithium is studied on four aged patients treated for endogenous depression. The patients were between 68 to 86 years old. They were all resistant to tricyclic and other antidepressants, MAO inhibitors and to lithium alone. The period of hospitalization varied between 1 1/2 to 3 years. After 4 weeks treatment with tryptophan a supplementary treatment with lithium was added. During the first month the ratio of tryptophan and the supplementary treatment with lithium was increased by the same ratio. The senile depression disappeared after 4 to 6 weeks combined treatment. During this period the pattern of aminoacids was studied. The positive results suggest further studies relating to deficiency of tryptophan in elderly patients with endogenous depression.

000497 Hervy, Ch.; de Basquiat, M.; Colas, N. Centre Hospitalier Regional, Limoges, France /**Asthe-crinol 12 in the asthenia syndrome of aged subjects.**/ L'asthe-crinol 12 dans le syndrome d'asthenie des sujets ages. Psychologie Medicale (Paris). 8(1):145-147, 1976.

Asthe-crinol 12 was studied in 30 hospitalized patients, 11 males and 19 females, ranging in age from 52 years old to 92 years old, all of whom had a significant asthenia. The asthenia was often associated with senile involution or with mental problems. Each patient received 1 ampule and 1 tablet of Asthe-crinol twice daily for 1 month. Good results were obtained in 17 patients, medium results in 9, and no results in 4. Short case descriptions are given of the 4 patients not responding. Patients with good results manifested return of appetite and interest in meals, personal care, and dress; better contact with others; and greater participation in conversation and certain activities. Tolerance was excellent with no side-effects noted. 5 references.

000498 Horyd, Wanda; Kuran, Wlodzimierz. Instytut Psychoneurologiczny, Sobieskiego 1/9, 02-957 Warszawa, Poland /**EEG pattern during L-dopa treatment of Parkinson's disease.**/ Obraz EEG podczas leczenia L-dopa chorych z zespolem Parksinsonowskim. Neurologia i Neurochirurgia Polska (Warszawa). 10(1):37-43, 1976.

Dynamics of EEG changes in 27 patients with Parkinson's disease treated with L-dopa were studied. The patients, 10 females and 17 males, ranged in age from 33-70 years (average age 55.4years), and the duration of illness was 2-13 years (average duration 5.5years). Pretreatment EEGs were compared with recordings made during clinical treatment and with clinical observations. Of eight cases with normal pretreatment EEG six showed improvement, and of 19 cases with abnormal pretreatment EEG 10 improved. Some intensification of temporal episodic complexes in EEG records was observed during treatment without concomitant changes in clinical manifestations. In two cases with slowed down background activity in the initial records, hallucinatory obnubilation developed, requiring withdrawal of treatment. This psychotic reaction was accompanied by greater slowing down of EEG activity. 9 references. (Author abstract modified)

000499 Isermann, H.; Haupt, R. Neurologisch-Psychiatrische Klinik der Krankenanstalten Sarepta, Bethel Bethesdaweg 11, D-4800 Bielefeld 13, West Germany /**Marked EEG changes during clozapine treatment of paranoid hallucinatory psychoses.**/ Auffallige EEG-Veranderungen unter Clozapin-Behandlung bei paranoid-halluzinatorischen Psychosen. Nervenarzt (Berlin). 47(4):268, 1976.

Treatment of 36 patients with endogenous paranoid/hallucinatory psychosis with the new neuroleptic clozapine (Leponex) caused a larger than anticipated increase in frequency and degree of paroxysmal dysrhythmia patterns in the electroencephalogram (EEG). Of this group, 26 patients exhibited a pathological EEG after at least 3 day's treatment, including paroxysmal dysrhythmia in 23 patients, general distortion in 15 patients, and in 8 patients convulsion like periods were observed in the form of abortive spike wave complexes. No organic brain convulsion occurred. In 19 patients, the EEG before drug administration showed pathological features in only two patients, whereas after clozapine 18 patients exhibited pathological changes, including 16 paroxysmal dysrhythmias. In comparison with the classic neuroleptics, pathological EEG changes under clozapine were much more clearly delineated. Within 3-5 days after commencement of treatment severe overall changes were noted, including groups of bilaterally synchronic, usually irregularly formed theta waves and delta waves of high amplitude. The manufacturer's claims that in comparison with other neuroleptics, EEG changes due to clozapine were small, and no change occurred in 50% of cases, cannot be confirmed. The often rapid improvement of paranoid/hallucinatory psychosis occurs almost simultaneously with the appearance of the pathological EEG changes.

000500 Kartzinel, Ronald; Hunt, Robert D.; Calne, Donald B. Bldg. 10, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD 20014 **Bromocriptine in Huntington chorea.** Archives of Neurology. 33(7):517-518, 1976.

The results of a study using bromocriptine in six hospitalized patients with Huntington chorea, a disease characterized by the appearance of involuntary movements and dementia, are presented. While bromocriptine has been shown to act as a postsynaptic, dopamine receptor agonist in rodent and primate models of Parkinsonism, it produced an increase in involuntary movements in HC patients. Adverse reactions included nausea and vomiting, agitation, confusion, irritability and somnolence. These side-effects cleared when bromocriptine was replaced with placebo. No changes in hematalogic or biochemical screening test results were found. Speculations on possible action mechanism of bromocriptine and the acting mechanisms of apomorphine, which has produced beneficial results, are made. It is concluded that the data supports the view that dopaminergic agonists ameliorate Parkinsonism and exacerbate chorea. 16 references.

000501 Kartzinel, Ronald; Shoulson, Ira; Calne, Donald B. National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, MD 20014 **Studies with bromocriptine: Part 2. Double-blind comparison with levodopa in idiopathic parkinsonism.** Neurology. 26(6,Pt.1):511-513, 1976.

A double-blind crossover study was performed in 12 patients with idiopathic parkinsonism to compare their response to bromocriptine with their response to previous optimal drug treatment, including levodopa. There was a 26% overall improvement with bromocriptine; rigidity, tremor, and facial expression showed the greatest response. Seven of eight patients who were taking levodopa at the beginning of the study were taken off the drug completely. Adverse reactions were transient and dose dependent. Bromocriptine is concluded to be an effective new therapeutic agent in the treatment of idiopathic parkinsonism. 20 references. (Journal abstract)

000502 Kudo, Y. no address **A double-blind comparison of lorazepam with diazepam in neurotic patients.** Medicina Psicosomatica (Roma). 20(4):429, 1975.

A double-blind comparative study of lorazepam with diazepam in 134 neurotic patients was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). It was noted that according to the physician's rating scale there was no significant difference between the two drug groups in relation to the global improvement rating and or in scores before and after the treatment of each item. According to the patient's rating scale, no significant difference was noted concerning the relative merits of the two drug groups in the blobal improvement rating, but in the cluster of anxiety symptoms diazepam was superior to lorazepam. Lorazepam, however, surpassed diazepam in the cluster of depressive symptoms and in the cluster somatic symptoms. It is concluded that though should be given to the indication of lorazepam in psychosomatic disease. (Author abstract modified)

000503 Lambert, P. Service Neurologie et Psychiatrie, Hospice Civil, 174, Avenue de Roosendael, F-59140, Dunkerque, France **/Noctran as a sleep inducer during hospitalization (based on 50 cases)./** Noctran en tant qu'inducteur du sommeil, au cours d'hospitalisations (a propos de cinquante cas). Psychologie Medicale (Paris). 8(3):469-474, 1976.

Noctran 10 was prescribed as sedative for hospitalized subjects who had difficulty sleeping as a consequence of a preexisting anxiety or anxiety associated with actual hospitalization. Results are on the whole satisfactory: improvement in sleep was recorded in 38 out of 50 subjects. The effect was mediocre in 10 cases and 2 cases were considered difficult to interpret. No unfavorable side effects were noted but 9 subjects had a tendency toward drowsiness the next morning. 13 references.

000504 Lugez-Renan, F. Universite de Lille, Lille, France **/Contribution to the clinical study of a new neuroleptic: sultopride./** Contribution a l'etude clinique d'un nouveau neuroleptique: le sultopride (MD dissertation). Lille, University of Lille MD dissertation, 1975. 127 p.

In an MD dissertation a trial of sultopride (Barnetil), a major tranquilizer of the anisamide class in 42 chronic psychotic patients is described. The daily dose ranged from 300mg to 1200mg, and was given im or orally. Results showed very good improvement in 23, good improvement in 9, slight improvement in 3, and no improvement in 7. Symptoms reduced by sultopride were manic excitation, agitation, aggressivity, hallucinations, mental automatism, delirium, and autism. Side-effects were extrapyramidal effects, plus depression in 11, anxiety in 7, and malicious syndrome in 3. In 7 patients treatment was interrupted because of side-effects.

000505 Marie-Cardine, M.; Merel, J.-P. no address **/Clinical trial of sultopride./** Essai clinique du sultopride. Psychologie Medicale (Paris). 8(5):800, 1976.

Sultopride (Barnetil) was studied in patients with typical mania and agitation crises. Sedative effects were very rapid. In one patient, mania was reduced so much within 48 hours that the patient could leave the hospital and rejoin his family on the 3rd day. It is concluded that sultopride is a well tolerated drug of strong and rapid action in manic states and agitation crises.

000506 May, Philip R. A.; Van Putten, Theodore; Yale, Coralee; Potepan, Penelope; Jenden, Donald J.; Fairchild, Mahlon D.; Goldstein, Michael J. Veterans Administration Hospital, Brentwood, Wilshire and Sawtelle Boulevards, Los Angeles, CA 90073 **Predicting individual responses to drug treatment in schizophrenia: a test dose model.** Journal of Nervous and Mental Disease. 162(3):177-183, 1976.

A test dose procedure is described which offers promise as a practical approach to selecting the most appropriate antipsychotic drug and dosage for a particular patient, and for tailoring blood concentrations to the needs of the individual case. Preliminary findings indicate that the test dose procedure is feasible; that detectable changes occur after a single test dose; and that measurements made during the test dose period may be predictive of eventual outcome. These findings are only a report of a preliminary pilot experiment, subject to important caveats about small number of cases, interpretation of large numbers of correlation coefficients, and need for cross-validation. Nevertheless, they are encouraging and suggest that the test dose approach has considerable potential for further research. 25 references. (Author abstract modified)

000507 Morandini, Graziella; Andreoli, Vittorino. no address **/Therapeutic advantages of a combination of neuroleptics with a new benzodiazepine: 7-chloro-5-(2-chlorophenyl)-1,3-dihydro-2H-1,4-benzodiazepin ne-2-one./** Vantaggi terapeutici di una associazione tra neurolettici e una nuova benzodiazepina: il 7-cloro-5-(2-clorofenil)-1,3-diidro-2H-1,4-benzodiazepin-2-o one. Lavoro Neuropsichiatrico (Roma). 56(1/2/3):201-213, 1975.

A clinical study was made to determine whether chlordemethyldiazepam can substitute in part for neuroleptic therapy. A group of 22 psychotic patients was given the Overall and Gorham rating scale during neuroleptic therapy, after 3 weeks of half dosage of neuroleptic plus chlordemethyldiazepam, and with half dosage of the neuroleptic. Results indicated chlordemethyldiazepam to be effective in controlling psychotic symptomatology when added to neuroleptic therapy, and increased dynamic activity of patients by reducing heavy side-effects through reduction of the neuroleptic dosage. 4 references. (Author abstract modified)

000508 Morandini, Graziella; andreoli, Vittorino. no address **/Possibility of using 7-chloro-5-(2-chlorophenyl)-1,3-dihydro-2H-1,4-benzodiazepin ne-2-one. in cases of psychotic symptomatology./** Possibilita di impiego nella sintomatologia psicotica del 7-cloro-5-(2-clorofenil)-1,3-diidro-2H-1,4-benzodiazepin-2-o one. Lavoro Neuropsichiatrico (Roma). 56(1/2/3):185-199, 1975.

A new drug, chlorodemethyldiazepam, was administered to 30 patients (7 females and 23 males, 18 to 70 years old) who showed psychotic symptomatology. In the double-blind study 10 patients received placebo, and the remainder were administered the drug. Results were evaluated by Hamilton's RSAS, Overall and Gorham's BPRS, and Wittenborn's rating scale, applied before and after the test. Improvement was noted in 60% of the cases, while worsening was reported with the placebo. 3 references. (Author abstract modified)

000509 Planche, R. Service de Neuro-Psychiatrie "B", Hopital General, 11, rue Sainte-Rose, F-63000 Clermont-Ferrand, France **/Study of the psychiatric indications of Lorazepam./** Etude des indications psychiatriques du Lorazepam. Psychologie Medicale (Paris). 8(1):133-143, 1976.

Lorazepam, a benzodiazepine derivative with antianxiety effects, was given to 36 patients, 35 males and 1 female. Of the patients, 12 were psychotic (4 melancholia, 4 schizophrenia, 1

acute psychosis, 3 chronic delirious psychosis), 20 were neurotic (8 neurotic state, 1 phobic neurosis, 1 obsessional neurosis, 8 neurotic depression, and 2 complex disequilibrium), and 4 had reaction states. All patients were hospitalized on the psychiatric service of a general hospital. They ranged in age from 21-years-old to 72-years-old. The dosage ranged from 2.5-10mg/day, with most patients receiving 7.5mg/day. The usual duration of treatment was 1-2 months, with a minimum of 8 days and a maximum of 1 year. In 10 cases, lorazepam was administered along with major tranquilizers, and in 18 cases, it was administered along with antidepressants. Good or very good results were obtained in 7 of the 12 psychotics and 8 of the 20 neurotics. Lorazepam was especially effective in mental anxiety, somatic anguish, and tension and excitement. The drug was well tolerated, the only side effect being reduced attention. No tendency toward addiction or dependence was noted. 38 references.

000510 Planche, R. Hopital General, 11, rue Sainte-Rose, F-63000 Clermont-Ferrand, France **/Treatment of psychiatric emergencies by a new neuroleptic: sultopride./** Traitement des urgences psychiatriques par un nouveau neuroleptique: le sultopride. Semaine des Hopitaux: Therapeutique (Paris). 52(4):261-262, 1976.

Two case studies are given illustrating the use of sultopride in the management of psychiatric emergencies (delirium, acute agitation). A dose of 1600mg/day parenterally was used initially in a 32-year-old male with mania, changing over to 3200mg/day orally by the 3rd week. Trihexyphenidyl in a dose of 15mg/day orally was also given. The patient was discharged after 32 days. A 25-year-old male with an episode of delirium was given 4800mg/day of sultopride orally, along with 15mg/day trihexyphenidyl and droperidol at night. He responded well to treatment by 15 days. In both cases sultopride was effective as a sedative and an antipsychotic and in reducing agitation in the patient.

000511 Puzynski, Stanislaw. II. Klinika Psychiatryczna Instytutu Psychoneurologicznego, Al. Sobieskiego 1/9, 02-957. Warsaw, Poland **/Standard method of evaluating mental state in clinical trials of psychotropic drugs./** Standardowe metody oceny stanu psychicznego w ocenie klinicznej lekow psychotropowych. Psychiatria Polska (Warszawa). 10(1):15-27, 1976.

Psychiatric and behavioral observation of patients in clinical drug trials are discussed. Methods vary in emphasis from the unspecific psychopathological viewpoint, such as general anxiety or emotionally unbalanced behavior, to focusing upon a particular symptom, such as insomnia or headache, and range to inventories and scales requiring physicians to use methods suitable for use by nurses and junior medical personnel. The methods and their application are discussed. 44 references.

000512 Resnick, Richard B.; Kestenbaum, Richard S.; Schwartz, Lee K.; Smith, Alfred. Division of Drug Abuse Research and Treatment, Department of Psychiatry, New York Medical College, 5 E. 102nd St., New York, NY 10029 **Evaluation of propranolol in opiate dependence.** Archives of General Psychiatry. 33(8):993-997, 1976.

A series of controlled, double-blind studies with hospitalized volunteers with histories of opiate dependence for from 4 to 8 years were carried out in order to validate the findings in beta adrenergic blocking drug research that propranolol hydrochloride (Inderal) is efficacious in the treatment of opiate dependence. The results of the studies do not confirm the previous reports. Propranolol neither relieved nor precipitated opiate withdrawal in subjects dependent either on dihydromorphinone hydrochloride or on heroin. It did not effectively block heroin induced euphoria in dependent or nondependent subjects. In addition, there was no effect on the pattern of self-administration in opiate dependent subjects, whether they were maintained on propranolol or placebo. 10 references. (Author abstract modified)

000513 Ross, S. B.; Jansa, S.; Wetterberg, L.; Fyro, B.; Hellner, B. Research Laboratories, Astra Lakemedel AB, S-15185 Sodertalje, Sweden **Decreased blood level of 5-hydroxytryptamine by inhibitors of the membranal 5-hydroxytryptamine uptake.** Life Sciences (Oxford). 19(2):205-210, 1976.

A study of the effect of chlorimipramine and (Z)-3-(4-bromophenyl)-N,N-dimethyl-3-(3-pyridyl)allyamine dihydrochloride (H 102/09) on the 5-hydroxytryptamine (5-HT) concentration in whole blood in rats and man is reported. Chlorimipramine and H 102/09 are known inhibitors of membranal 5-HT uptake. In rats chlorimipramine had a slight but significant effect on the 5-HT concentration in the rat blood and on the 5-HT uptake in brain slices. H 102/09 caused a marked decrease in the 5-HT concentration after 2 days treatment. The effect on the blood 5-HT concentration was obtained at the same dose level producing marked inhibition of the 5-HT uptake in hypothalamic slices. In man therapeutic dosage of chlorimipramine and H 102/09 caused a strong decrease in the blood 5-HT concentration after two weeks treatment. Determination of the 5-HT concentration in whole blood may be a valuable test of the in vivo effectiveness of inhibitors of the 5-HT uptake under clinical conditions. 23 references. (Journal abstract modified)

000514 19(2):205-210, 1976. Gouin, Paul R.; Tower, Barbara B. Neurology Laboratory, UCLA School of Medicine, Harbor General Hospital Campus, Torrance, CA 90509 **Selective neuroendocrine effects of low-dose haloperidol in normal adult men.** Psychopharmacology (Berlin). 47(2):135-140, 1976.

The neuroendocrine effects of haloperidol, usually reported as side effects of this drug when given in antipsychotic doses, are systematically investigated. Five normal adult men were administered saline and two doses of haloperidol (0.25mg, 0.5mg) intramuscularly in a double-blind randomized block design. The anterior pituitary hormones -- luteinizing (LH), growth hormone (GH), follicle stimulating hormone (FSH), and prolactin release (PRL) -- were measured in blood samples taken every 20 min for several hours thereafter. The low doses of haloperidol used have been shown by others to alter the human EEG; in these subjects the doses produced no objective or subjective clinical effects. There were no drug related changes in GH, LH, or FSH; PRL, however, showed a prompt, statistically significant, dose related increase in plasma levels, with a return to baseline within 5 hours. Haloperidol has strong dopamine blocking effects, and the hypothalamic inhibitory mechanism for PRL release is believed to be dopamine mediated. Results suggest that haloperidol may have utility in low doses primarily for its hypothalamic neuroendocrine effects, and that dose related PRL release may be a useful paradigm for comparing dopamine blocking antipsychotic agents in humans. 38 references. (Author abstract modified)

000515 Sandler, K.; Digiacomo, J.; Mendels, J. Department of Psychiatry, Veterans Administration Hospital, Philadelphia, PA 19104 **Evaluation of lenperone in acute schizophrenia.** Current Therapeutic Research. 20(4):549-541, 1976.

Eleven newly hospitalized schizophrenics were treated with lenperone (AHR-2277) a butyrophenone, and results are summarized. The eight subjects who completed the study showed definite improvement in a broad range of symptomatology when treated with 10 to 100 milligrams of lenperone over 30 days. Results provide preliminary evidence that lenperone may be an effective antipsychotic agent with a relatively low incidence of extrapyramidal effects. 9 references. (Journal abstract modified)

000516 Scharbach, H. Centre Hospitalier, Verdun F-55017, France **/Beta-blockers as psychotropic drugs./** Les beta-bloqueurs comme psychotropes. Encephale (Paris). 2(1):85-101, 1976.

A screening of two beta-blocking substances (alprenolol and pindolol) was carried out on 58 patients. The initial target symptoms were anxiety and psychosomatic manifestations. Results indicate that alprenolol and pindolol appear to have a central psychotropic action: anxiolytic but nonsedative; thymoleptic, increasing the incitement to action yet normalizing certain excited states; increasing attention level and exploration of surroundings; decreasing autoaggressive heteroaggressive manifestations. No significant antidelusion or antihallucination action was noted. 62 references (Author abstract modified)

000517 Sellman, R.; Kanto, J.; Raijola, E.; Pekkarinen, A. Dept. of Pharmacology, Turku University, Kiinamyllynkatu 10, Turku 52, Finland **Induction effect of diazepam on its own metabolism.** Acta Pharmacologica et Toxicologica (Kobenhavn). 37(5):345-351, 1975.

In the seven psychiatric patients 10mg diazepam administered in travenously, during continuous therapy, caused a significantly lower increase of diazepam concentrations in the plasma (at 15 min, P less than 0.01; 1 hour, P less than 0.001; 3 and 6 hours P less than 0.05; 24 hours, P less than 0.001) than in 13 healthy volunteers as an indicator of the increased elimination rate of diazepam. As a sign of the increased formation of the main metabolite, the increase in the concentration of N-demethyldiazepam was significantly higher in the psychiatric patients on continuous diazepam therapy (at 15 min, P less than 0.05; 1 hour, P less than 0.01) than in healthy volunteers. The intravenous injection of 10mg diazepam caused in seven psychiatric patients on continous diazepam therapy a significantly lower mean increase of diazepam concentrations in the plasma (at 15 min, 1 hour, 3 and 6 hours P less than 0.01; 24 hours, P less than 0.001) than in 12 psychiatric patients treated without diazepam (at 1 hour P less than 0.05). No measurable amounts of free oxazepam was found in the plasma. 18 references. (Author abstract)

000518 Smith, James; Misiak, Henryk. Office of Clinical Research, Harlem Valley Psychiatric Center, Station A, Wingdale, NY 12594 **Critical flicker frequency (CFF) and psychotropic drugs in normal human subjects -- a review.** Psychopharmacology (Berlin). 47(2):175-182, 1976.

This literature review presents summary methodological and statistical data on 33 studies in which critical flicker frequency (CFF) thresholds were used to evaluate the effects of acute oral doses of single psychotropic drugs in normal human subjects. In all, 96 drug dose study combinations are represented. CFF was found to be altered to a statistically significant degree in 51 (65%) of the 79 instances in which inferential statistical methods were used to evaluate the results. As expected, stimulants increased CFF while hypnotics decreased it. There is also a discussion of important methodological considerations in the design of psychopharmacological studies employing CFF. While many studies have shown CFF to be sensitive to the effects of psychotropic drugs, there have not always been adequate controls for extraneous factors (especially, set and suggestion, changes in pupillary diameter, and the presence of other commonly used drugs). Finally, consideration is given to the attempts to increase the sensitivity of the CFF test to drug effect. 69 references. (Author abstract)

000519 Soderholm, S.; Viukari, N. M. A.; Rimon, R. Psychiatric Clinic, Univ.-Central Hospital Lapinlahti SF-00181, Helsinki 18, Finland **/Psychotropic effect of pyrovalerone (F-1983), placebo, and milieu therapy and the pyschological status of forensic psychiatric patients./** Die psychotrope Wirkung von Pyrovalerone (F-1983), Placebo, Milieutherapie und psychischer Zustand bei gerichtspsychiatrischen Patienten. Nervenarzt (Berlin). 47(2):88-93, 1976.

In a double-blind crossover study in the psychiatric ward of a prison, to determine whether pyrovalerone (Centroton) has psychotropic properties, it was found pyrovalerone influenced test performance of patients significantly more than placebo, although due to its stimulating effect it also significantly increased feelings of anxiety. The placebo did not cause anxiety. Placebo had a greater effect on the insecurities of the medication group than simple confinement on the psychodiagnostic ward (milieu therapy) had on the control group. No signs of dependency or withdrawal symptoms could be established for pyrovalerone and it showed less side-effect than the placebo, although this distinction was not statistically significant. The results show that court confined patients react with feelings of anxiety and inner tension as soon as they are subjected to treatment measures, even though they can profit from the treatment. The attitude of the hospital staff was astonishingly negative during this attempt at medication. Male patients in Finland, for whom the forensic psychiatric investigation was ordered, are usually schizoid, depressive, psychasthenic, sociopathic, paranoid, or exhibit a certain degree of hysterical personality. 11 references. (Author abstract modified)

000520 Sutter, Jean M. Clinique de Psychiatrie, Hopital de la Timone, Boulevard Jean-Moulin, F-13005 Marseille, France **/The benzamides in psychopharmacology: sulpiride and sultopride./** Les benzamides en psychopharmacologie: sulpiride et sultopride. Psychologie Medicale (Paris). 8(2):293-303, 1976.

The pharmacology of sulpiride and sultopride, two benzamide derivatives, is discussed. Chemical structures are given for 4 benzamides: metoclopramide (Primperan), sulpiride (Dogmatil), sultopride (Lon 1418), and tiapride. Sulpiride was given to 112 patients, 49 men and 63 women. The first week, they received 300-400mg i.m. daily, and the following 3 weeks, they received 1200mg/day orally. Diagnoses were schizophrenia in 67, nonschizophrenic delirious psychoses in 36 (12 acute, 24 chronic), and depressive psychoses in 9. Good results occurred in 10 acute delirious psychotics, half of the chronic delirious psychotics, and 32 schizophrenics. In another experiment, sultopride was given to 30 patients, of which 2 were acutely delirious, 1 was chronically delirious, and 27 were schizophrenic. The subjects were all male and ranged in age from 19 years old to 70 years old, nearly all being under 40 years old. Half of the schizophrenics had been ill less than 5 years. Patients the first few days received daily doses of 800mg parenterally, and after that 800-3600mg/day orally. Results were good in 11, medium or slight in 9, no effect in 8, and aggravation in 2. These results were observed at the end of 28 days of treatment. Side-effects of sulpiride were extrapyramidal effects, insomnia, galactorrhea, and amenorrhea,

and occasionally orthostatic hypotension and vertigo. Side-effects of sultopride were extrapyramidal effects, somnolence, galactorrhea, and depression. No development of addiction occurred. 20 references.

000521 Szasz, Thomas. Upstate Medical Center, Syracuse, NY **/Psychiatrists, physicians and the CIA drug program./** Patriotic poisoners. Humanist. 36(6):5-7, 1976.

The role of physicians and psychiatrists in drug trials sponsored by the Central Intelligenc Agency (CIA) is questioned and denounced. The Rockefeller Commission's "Report on CIA Activities Within the United States" (1975) indicates that the CIA studied drugs as one means of controlling human behavior and that one test subject jumped from a window and died after being administered LSD. Other examples of fatality and derangement associated with drug trials are summarized. The physicians known to have participated in the drug trials are or were psychiatrists. It is concluded that they are implicated in violations of medical ethics and criminal (drug) law. 16 references.

000522 Tsukasaki, Naoki. no address **Evaluation of the new drug – clomipramine (anafranil).** Psychiatria et Neurologia Japonica (Tokyo). 77(10):737-744, 1975.

It is noted that new drugs are often advertised in Japan, despite conflicting preclinical and clinical evaluations regarding effectiveness, side-effects, and toxicity. In the evaluation of clomipramine (anafranil), problems such as acute and chronic toxicity and acceleration of abnormality were noted. Nevertheless, the drug has been given to young females. It is recommended that more accurate and precise preclinical and clinical experiemnts be conducted before putting new drugs on the market. 35 references.

000523 Yaryura-Tobias, J. A.; Neziroglu, F.; Bergman, L. North Nassau Mental Health Center, Manhasset, Long Island, NY 11030 **Chlorimipramine, for obsessive-compulsive neurosis: an organic approach.** Current Therapeutic Research. 20(4):541-548, 1976.

A new compound, chlorimipramine, a tricyclical antidepressant, was used on obsessive-compulsive neurotics (18 patients) and on psychotics with obsessive-compulsive symptomatology (10 patients), and results are summarized. With the neurotics, a 4 month double-blind study was used, and with the psychotics, an open study of 8 weeks. Improvement was rated on several scales, including the Brief Psychiatric Rating Scale, Clinical Global Impression, Hamilton Depression Scale, and the Obsessive-Compulsive Inventory. Results indicated significant improvement on all scales with neurotics at termination; with psychotics, a decrease in anxiety caused by rituals was noted. A serotonergic disturbance is proposed as a causative factor for this illness. 31 references. (Journal abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

000524 Agedaira, Tadaya. Department of Neuropsychiatry, Hachido Municipal Shimin Hospital, Japan **Clinical experience in using TLP-607 (Penfluridol) for acute schizophrenia.** Medical Consultation & New Remedies (Tokyo). 12(7):1553-1562, 1975.

Penfluridol (TLP-607) was tested on eight schizophrenics and two cases of unspecified mental illness. Dosage was between 20-30 mg, but administration was varied to be either once per week, once every 5 days, or in some cases twice weekly. Penfluridol was deemed very effective in one case, effective in five, and uneffective in four cases giving it an overally effectiveness of 60%. In all of the effective cases, it was used to quiet the abnormal experiences of patients in acute phases of schizophrenia. It didn't, however, have much effect on auditory hallucinations, delusions, or against abnormalities such as tension confusion, or excitedness. Transitory side-effects were noted in one case. It was thought that if major symptoms reoccurred, TLP should be used in conjunction with a major tranquilizer.

000525 Altschule, Mark D.; Bigelow, Llewellyn B.; Bird, Robert M.; Bliss, Eugene L.; Cancro, Robert; Gjessing, Leiv R.; Kety, Seymour; Lipton, Morris. Harvard Medical School, Boston, MA **The nature of schizophrenia.** In: Wolf, S., The biology of the schizophrenic process. New York, Plenum, 1975. 199 p. (p. 16-39).

In a discussion conducted at the Totts Gap, PA, Colloquium on the Biology of Schizophrenia, May, 1975, the nature of the disorder, including its biological and behavioral characteristics, genetic aspects, developmental processes, diagnosis, treatment, and incidence was examined. Although contradictory positions were noted on these issues, major theoretical and experimental points included: 1) the existence of the disorder as a psychosomatic orientation, with a biological defect expressed behaviorally in the individual who has been conditioned by early deleterious experiences; 2) the multiple etiology of schizophrenia, in both its latent and active forms, as a disorder which distorts mental and emotional behaviors and is characterized by dissociation and disorganization of adaptive responses; 3) the differences in schizophrenic and normal psychophysiological and metabolic responses to stress phenomena; 4) the significance of the label, schizophrenia, and its diagnostic considerations as compared to other mental disorders such as mental retardation; 5) the validity of viewing schizophrenic behavior as a normal variant, as suggested in Szasz' arguments regarding the undesirable social consequences of the term's use; 6) the importance of selecting the proper patient sample when studying new therapeutic approaches and distinguishing between acute schizophrenic reaction and schizophrenia with acute onset; 7) the reversibility of the schizophrenia syndrome with psychotropic drug treatment, particularly with chlorpromazine; 8) the continuing search for specific features by which to identify schizophrenia as a disease; 9) the nature of creativity among schizophrenics; 10) the epidemiological aspects of the disorder; and 11) the increasing productivity of community residing schizophrenics.

000526 Altschule, Mark D.; Bigelow, Llewellyn B.; Bliss, Eugene L.; Cancro, Robert; Gjessing, Leiv R.; Kety, Seymour; Lipton, Morris; Snyder, Solomon. Harvard Medical School, Boston, MA **/Pharmacologic therapy for schizophrenia./** Therapy. In: Wolf, S., The Biology of the Schizophrenic Process. New York, Plenum, 1975. 199 p. (p. 151-160).

In a discussion conducted at the Totts Gap (Pa.)Colloquium on the Biology of Schizophrenia, May, 1975, considerations in treating the disorder with phenotiazines were treated, and data on the relative potency of neuroleptics in schizophrenia and affective disorders were presented. It appears that antischizophrenic drugs are effective in treating depression as well, but additional analyses suggest that neuroleptics such as the phenothiazines and related drugs do not have the desired systemic effects of the tricyclics in retarding endogenous depression or the benefit in treating anxiety of thioridazine and chlorpromazine. Studies of the effects of lithium therapy in schizophrenia indicate that it may be beneficial in some cases but that effects vary. Some of the similarities in

psychotropic treatment effects in schizophrenia and depression are attributed to affective features of the former disorder which have been of historical interest to theorists and practitioners. Although the subject is controversial, there is a possibility that there is a single psychosis which is alternately called schizophrenia and depression, and most clinical research at least suggests that schizophrenia is a very complex phenomenon in both its biological and psychological entities.

000527 Altschule, Mark D.; Bigelow, Llewellyn B.; Gjessing, Leiv R.; Lipton, Morris; Synder, S.; Wolf, Stewart; Wyatt, R. Harvard Medical School, Boston, MA **Clinical investigations.** In: Wolf, S., The Biology of the Schizophrenic Process. New York, Plenum, 1975. 199 p. (p. 104-133).

In a discussion conducted at the Totts Gap (Pa.)Colloquium on the Biology of Schizophrenia, May, 1975, a newly developed nurses' rating scale for schizophrenic behavior was described, and results from its use with an etiologically homogeneous group of inpatients were presented. The scale covers a wide range of expressed psychopathology and, unlike the NOSIE, there are no items representing positive achievement so that staff cannot reward patients. Questions are more general than the NOSIE and have been rated more useful by day shift and night shift nurses who have used them. Behaviors which encompass a psychosis rating for each patient include loss of emotions, disorganized speech form, delusional statements, bizarre behavior, and hallucinations (statements and behaviors). The scale was applied to the experience of two patients who were treated with 5-hydroxytryptophol (5-HTP) and aqueous pineal extract protocols to demonstrate that progress in understanding and treating schizophrenic patients can only come from individual case study since the disorder is a syndrome with diverse etiologies. Data on the behavioral effects of the hypothalamic polypeptides and thyrotropin releasing hormone and their use in schizophrenia were also reviewed.

000528 Altschule, Mark D.; Bigelow, Llewellyn B.; Bliss, Eugene L.; Cancro, Robert; Cohen, G.; Gjessing, Leiv R.; Haber, B.; Kety, Seymour; Lipton, Morris. Harvard Medical School, Boston, MA **Pathophysiology -- biochemical considerations.** In: Wolf, S., The Biology of the Schizophrenic Process. New York, Plenum, 1975. 199 p. (p. 81-103).

In a discussion conducted at the Totts Gap (Pa.)Colloquium on the Biology of Schizophrenia, May, 1975, data were presented on the role of neurotransmitters and biochemical mechanisms, as well as the actions of psychotropic drugs, in schizophrenic behavior. Research data indicate that the phenothiazines block dopamine receptors; that amphetamines exacerbate schizophrenic symptoms and produce schizophrenia like psychoses; and that antidepressant agents such as the tricyclics produce side effects similar to amphetamine psychosis. The amphetamine actions are apparently dependent on catecholamines, especially dopamine (DA), and administration of the amino acid precursor of DA, L-DOPA, worsens schizophrenic symptoms. More recent findings suggest that methyphenidate (Ritalin) acts preferentially on DA neurons as contrasted to amphetamines which act preferentially on norepinephrine (NE), and that the worsening of schizophrenic symptoms by amphetamine may be mediated by DA as opposed to NE. Current theories that phenothiazines primarily block at DA receptors and that the blockage correlates with their clinical effectiveness were reviewed, along with evidence of the therapeutic effectiveness of the butyrophenones and phenothiazines in treating the various types of schizophrenia (including the sedative versus antipsychotic effects of the phenothiazines) was cited. Studies of platelet MAO versus brain MAO in schizophrenics, in which genetically determined differences in enzyme activity were demonstrated in schizophrenics, were then treated.

000529 Anderson, William H.; Kuehnle, John C. Massachusetts General Hospital, Boston, MA **Dosage for antipsychotic drugs** New England Journal of Medicine. 295(3):173-174, 1976.

A flexible dosage protocol in 24 acutely manic or schizophrenic patients using intramuscular haloperidol in reported. No evidence for consistent superiority of high doses was found but a highly individual dose response in 11 patients who achieved remission on doses of 10-45mg is noted. Agreement with other investigators who recommend flexible dose strategy in administering antipsychotics is offered contingent on constant clinical monitoring of therapeutic response vs side effects. It appears that maintenance dosage will be a fraction of remission inducing dosage although wide individual variation may be anticipated.

000530 Andrews, P.; Hall, J. N.; Snaith, R. P. Stanley Royd Hospital, Wakefield, Yorkshire, England **A controlled trial of phenothiazine withdrawal in chronic schizophrenic patients.** British Journal of Psychiatry (London). 128:451-455, 1976.

Phenothiazine drugs were withdrawn from 17 chronic schizophrenic inpatients, with a control group of 14 patients remaining on active medication. The trial was conducted under double-blind conditions over a period of 42 weeks with weekly assessment of the patients by ward nurses. Of the placebo group 35% relapsed, relapse being related to the level of previous active medication. It is suggested that large numbers of chronic schizophrenic patients are maintained on phenothiazine drugs without deriving any benefit. All such patients, especially those receiving doses equivalent to less than 200mg of chlorpromazine daily, should be periodically withdrawn from drugs. Medication should, however, be immediately available to those patients who are clearly relapsing. 9 references. (Author abstract modified)

000531 Asada, S.; Ishimaru, T.; Kubo, S.; Kodama, H.; Masuda, K.; Kawamura, T.; Nomura, S.; Miyake, Y.; Tsukue, I.; Ishikawa, H.; Sasaki, T.; Jitsuiki, S. Asada Psychiatric Hospital, Hiroshima, Japan **/Study on the effects of Sulpiride and Perphenazine in 82 schizophrenics using the double-blind method./** Etude des effets cliniques du Sulpiride et de la Perphenazine chez 82 schizophrenes par la methode du double aveugle. Encephale (Paris). 2(1):73-83, 1976.

A clinical and statistical evaluation of Sulpiride and Perphenazine was carried out through a double-blind study of 82 schizophrenic patients of both sexes aged 20 years old to 56 years old. All were chronic patients with a symptomatic profile of apathy and lack of initiative but with personality relatively well preserved in 56 patients. The daily dosage varied from 300-1200mg Sulpiride orally and 12-48mg Perphenazine. The therapeutic effects were compared both individually and globally at different points in time over a 10 week period. Using Armitage's restricted sequential design, no significant difference between the therapeutic effects of these 2 neuroleptics was noted. However, Sulpiride appeared more beneficial during the 4th and 8th weeks of treatment. (Author abstract modified)

000532 Athen, D.; Bente, D.; Bikadorow, V.; Feder, J.; Muller-Oerlinghausen, B. Universitats-Nervenklinik, Nussbaumstrasse 7, 8 Munchen 15, Germany **/Clinical spectrum of**

action of moderate and high doses of Carpipramine./ Das klinische Wirkungsspektrum mittlerer und hoher Dosen von Carpipramin. Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 8(5):296-309, 1975.

An open trial of Carpipramine was made in a group of 75 acute and chronic schizophrenic patients (44 males, average age 30; 31 females, average age 33) over a period of 30 days. The daily dose was between 400mg and 800mg, exceeding the recommendations of the manufacturer. Carpipramine is a synthesis of the basic ring structure of a tricyclic antidepressant with a side chain of butyrophrenone. Psychopathological changes were documented and evaluated by the AMP and AMPAS symptom rating scales. The trial was completed in 50 of the patients. By the 10th day only the productive symptoms and sleep disturbance showed significant decrease. The symptom of somatic hallucinations responded especially well and quickly to treatment with Carpipramine. Anticholinergic effects were moderate. Evidence points to a slight centrally stimulating component. This drug can not be definitely classified as either a typical neuroleptic or antidepressant. A differential action depending on the initial syndrome constellation is also discussed. 11 references. (Author abstract modified)

000533 Bellak, Leopold. Albert Einstein College of Medicine, New York, NY **A possible subgroup of the schizophrenic syndrome and implications for treatment.** American Journal of Psychotherapy. 30(2):194-205, 1976.

A study of 20 schizophrenic patients and their extended families provides data to support the hypothesis that minimal brain dysfunction (MBD) is the major etiologic and pathogenic factor for one subgroup of adult schizophrenics and provides data on treatment. The cortical problems created by MBD lead to problems of establishing self-boundaries and coordination, to feelings of perplexity, difficulties with written and spoken words and abstract conceptualization, poor impulse control and defenses, overload by external stimuli and resulting disorganization. These phenomena in turn can cause secondary emotional problems, especially during the school years. This group is diagnostically characterized by a poor response to phenothiazines alone. Therapeutically, energizers together with diphenylhydantoin and haloperidol are often useful. Prevention of overload and genetic counseling may be indicated. 23 references. (Author abstract modified)

000534 Bigelow, Llewellyn B. NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Baclofen treatment in chronic schizophrenia (unpublished paper).** Bethesda, MD, NIMH, 1976. 1 p.

Hospitalized treatment resistant chronic schizophrenics were given baclofen administrations in a controlled double-blind experiment to determine if the drug possesses antipsychotic activity. Seven patients completed the protocol, which called for stabilization on optimal phenothiazine regimen and month long periods of treatment with placebo and baclofen in doses to 80mg/24 hr in a crossover design. Possible transitory improvement was observed in two subjects and deterioration was noted in two subjects. Findings do not confirm the experience of Frederikson (1975) and suggest that baclofen is not indicated in treating schizophrenia. The negative results have theoretical interest, however, in view of the recent surge in interest in substance P, which is an undecapeptide with varying regional distribution in the brain and which acts as a modulator of synaptic transmission.

000535 Bigelow, Llewellyn B.; Bird, Robert M.; Cancro, Robert; Cohen, G.; Gjessing, Leiv R.; Goldstein, A.; Kety, Seymour; Lipton, Morris; Werthessen, N. Mental Health Research, St. Elizabeth's Hospital, Washington, DC **Etiological considerations.** In: Wolf, S., The Biology of the Schizophrenic Process. New York, Plenum, 1975. 199 p. (p. 134-150).

In a discussion conducted at the Totts Gap (Pa.)Colloquium on the Biology of Schizophrenia, May, 1975, the possibility of a viral etiology which could account for the genetic patterns seen in chronic forms of the disorder was discussed. Results from animal models are cited, and it is contended that Koch's postulates need not be met literally to prove a viral etiology for certain human diseases. Criterion for acceptance would be the demonstration in more than one laboratory that the disease can be consistently transmitted to experimental animals or that a particular virus can be recovered consistently from the diseased cultures in vitro; that the disease can be serially transmitted to animals with untrafiltered material from the diseased S; and that the agent in question is not ubiquitous or being carried along as a passenger or contaminant. Three major lymphocyte cell populations involved in the pathogenesis of autoimmune mechanisms were identified, and results of immunological research with schizophrenics were presented in support of this view. Discussion centered around the effect of cortisone, megavitamins, other drugs in treating schizophrenia, and various animal models of schizophrenic behavior which have implications for therapeutic environmental manipulation and psychopharmacologic treatment.

000536 Brambilla, F.; Guerrini, A.; Rovere, C.; Guastalla, A.; Riggi, F.; Recchia, M. Ospedale Psichiatrico Paolo Pini, Via Ippocrate 45, I-20161 Milano Affori, Italy **Growth hormone secretion in chronic schizophrenia.** Neuropsychobiology (Basel). 1(5):267-276, 1975.

The growth hormone (GH) response to insulin hypoglycemia was studied under basal conditions and during a course of haloperidol therapy in 19 chronic schizophrenics, 15 hebephrenics, and four paranoids. Haloperidol was given for 30 days, and the GH response to the insulin induced hypoglycemia was tested twice before and 10, 20, and 30 days following initiation of the treatment. The psychopathological features were controlled daily by two psychiatrists and by the ward staff and by the use of the Wittenborn rating scale, rated at the same intervals as the hormonal assays. From the results obtained it appears that schizophrenic patients, GH secretion and response to insulin stimulus are extremely variable and are unaffected by haloperidol treatment. On the basis of the results, the neurotransmitter/neurohormone regulation of GH secretion in schizophrenics is discussed. 29 references. (Author abstract)

000537 Buchanan, F. H.; Parton, R. V.; Warren, J. W.; Baker, E. P. John Edis Hospital, Creek Road, New Town 7008, Tasmania **Double blind trial of L-dopa in chronic schizophrenia.** Australian and New Zealand Journal of Psychiatry (Carlton). 9(4):269-271, 1975.

A double-blind study of 28 chronzc schizophrenics was carried out comparing L-dopa with placebo (both groups continuing to receive regular neuroleptic medication) over a 6 week period. Assessments by psychiatrists and a psychologist using the Rockland and Pollin Rating Scale showed differential improvement of insignificant proportions, but the nurse's ratings showed clearly significant improvement in the subject group. 6 references. (Author abstract)

000538 Ciurezu, T.; Ionescu, Rodica; Udangiu, St. Nica; Niturad, D.; Oproiu, Liana; Tudorache, Dana; Popovici, Ile-

ana; Curelaru, Silvia. Clinique de Psychiatrie de l'Hopital "Gh. Marinescu," Bucarest, Romania **/Double-blind clinical comparison of HF-1854 (LX 100-129, clozapine, or leponex) with haloperidol./** Etude clinique en "double blind" du HF 1854 (= LX 100-129 = clozapine = leponex) compare a l'haloperidol. Neurologie et Psychiatrie (Bucuresti). 14(1):29-34, 1976.

A double-blind comparison was made of HF-1854 and haloperidol in two groups of 20 schizophrenic patinets each. The antipsychotic and the modular effects of HF-1854 were demonstrated. It had more rapid action, was better tolerated and produced more constant resocialization than haloperidol. There were no significant statistical differences between the pretherapeutic and posttherapeutic scores of patients treated with the two drugs. When no extrapyramidal phenomena are noted, HF-1854 can also be given to outpatients or semiconfined patients, with perspectives of amelioration of behavior and of lasting social and professional reintegration. 8 references.

000539 Davis, K. L.; Hollister, L. E.; Berger, P. A. Veterans Administration Hospital, Palo Alto, CA 94304 **Baclofen in schizophrenia.** Lancet (London). 1(7971):1245, 1976.

Contrary to reports in the literature 4 newly admitted schizophrenic patients treated with baclofen, a homolog of gamina-aminobutyric acid (GABA), reaching peak doses of 80-100mg/day were worsened by the drug. The worsening of thought and behavioral disorders was pronounced. While baclofen has no effect on GABA content, glutamic-decarboxylase activity, monoamine-oxidase activity or catecholamine content of the brain, its structural similarity to phenethylamine, a potential and endogenous psychotogen, may be pertinent.

000540 Devlin, D. no address **Acute psychotic episode in a chronic paranoid personality.** Nursing Times (London). 72(19):750-751, 1976.

The course of inpatient treatment of a woman diagnosed as having an acute psychotic episode with a chronic paranoid personality is described. It was her sixth admission for acute psychotic episodes in seven years. Therapy included chlorpromazine, nitrazepam and electroconvulsive therapy. The attendants on the ward were instructed to encourage her to talk about her persecutory delusions in an understanding and noncontradictory way as her friends, and be alert to interests in activities and outside realities. She was released with the knowledge that another psychotic phase might require rehospitalization. 1 reference.

000541 Dube, K. C.; Kumar, Narender. Research Unit, Mental Hospital, Agra, India **Loxapine succinate: a comparative study with chlorpromazine.** Current Therapeutic Research. 19(6):653-660, 1976.

Clinical effectiveness of loxapine succinate, a new neuroleptic agent and tricyclic dibenzoxazepine derivative, was compared with chlorpromazine during a 12 week double-blind study on 52 patients hospitalized with symptoms of functional psychoses. Remarkable improvement was noticed in both treatment groups. Total Brief Psychiatric Rating Scale scores showed no significant difference between the improvement of the groups. Item wise significant differences were observed in symptoms of tension, depressive mood, and motor retardation where chlorpromazine showed more improvement. The loxapine group consisted of significantly more chronic cases than the chlorpromazine group, and this may account for the difference. A continuous decrease in global severity from initial to final stage was observed without any significant intergroup differences. The optimal dosage range was 20 to 80mg/day and 200mg/day to 800mg/day for loxapine and chlorpromazine, respectively. On this dosage regimen, there was no evidence of side effects. 8 references. (Author abstract modified)

000542 Forsen, Alf; Pirttipera, Vaino. Roparnas Sjukhus, SF-65320 VASA 32, Finland **/Intramuscular double-blind study of depot-treatment of fluspirilene and fluphenazine in chronic schizophrenia./** Jamforande dubbelblindundersokning av depaadministration av fluspirilene och flufenazinenantat vid kronisk schizofreni. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(8):665-671, 1975.

In a double-blind crossover comparison, the two depot drugs fluspirilene and fluphenazine, were studied. The trial comprised 41 patients hospitalized for schizophrenia for more than 15 years. Five patients interrupted the treatment. The previous peroral neuroleptic medication was cut off 3 days before the trial. A data analysis showed a significant improvement for both drugs as to social capability, especially during the first weeks. Fluspirilene decreased retardation. Fluphenazine showed a significant improvement of the psychotic symptoms. Fluphenazine gave more extrapyramidal secondary effects qualitatively as well as quantitatively. No pathological findings were registered. 11 references.

000543 Garver, David L.; Davis, John M.; Dekirmenjian, Haroutune; Ericksen, Stephen; Gosenfeld, Lawrence; Haraszti, Joseph. Illinois State Psychiatric Institute, 1601 West Taylor Street, Chicago, IL 60612 **Dystonic reactions following neuroleptics: time course and proposed mechanisms.** Psychopharmacology (Berlin). 47(2):199-201, 1976.

The occurrence of acute dystonic reactions was studied relative to drug pharmacokinetic parameters including torticollis, retrocollis, opisthotonus, and oculogyrus following a single dose of the phenothiazine, butaperazine. Dystonias occurred more than one half-life from peak butaperazine levels, 23 h to 56 h after drug administration. The appearance of dystonias on falling plasma concentrations may be due to disruption of dopaminergic/cholinergic balance caused by differential antidopaminergic and anticholinergic potencies of the drug. The regular occurrence of dystonic reactions, which appear many hours after peak levels and on falling plasma and presumably brain concentrations of drug, may be result of a temporary disruption of cholinergic/dopaminergic balance in the direction of cholinergic dominance. There is as yet no direct evidence to favor this hypothesis rather than alternate hypotheses concerning, for example, temporary overshooting by compensatory mechanisms following dopaminergic blockade. However, a period of temporary cholinergic dominance accompanied by a display of extrapyramidal symptoms on falling drug concentrations might be predicted from knowledge of relative antidopaminergic and anticholinergic potencies of this group of neuroleptics. 6 references. (Author abstract modified)

000544 Haase, H. J. Pfalzische Nervenklinik Landeck, Germany **The relation of the action of neuroleptic drugs to the extrapyramidal system and the effectiveness of long-acting neuroleptic drugs for the treatment of schizophrenic patients.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(8):951-959, 1975.

The effect of neuroleptics on the extrapyramidal system of schizophrenics is reported. Three hundred twenty eight schizophrenics were administered neuroleptics and their handwriting was studied as the drug dosage was increased. It was found that the neuroleptic threshold was generally obtained

during the first 2 or 3 days and was most effective in the first 6 days. It is maintained that a definite relationship between neuroleptic threshold and extrapyramidal fine motor phenomena exists, and a sufficient neuroleptic potency was necessary to reach the threshold. A table consisting of low, medium, and neuroleptic potencies, and the required dosages to attain the thresholds is established with chlorpromazine as a baseline. Problems arising from prolonged use of neuroleptics, such as suicide and the necessity for outpatient guidance and care are also discussed.

000545 Haraoka, Yoichi; Tsukamoto, Ryuzo; Mizuno, Kazuko. Department of Psychiatry, Asahikawa Municipal Hospital, Japan **Clinical experiences in using high dosages of Fluphenazine enanthate and Fluphenazine on schizophrenia.** Medical Consultation & New Remedies (Tokyo). 12(9):2175-2182, 1975.

Fluphenazine enanthate (FE) and Fluphenazine (FL) were administered in high doses to 22 schizophrenic patients. It was found very effective in three cases, effective in six, slightly effective in five, and ineffective in eight cases, giving it an overall effectiveness of 63%. Both FE and FL were found to have about the same effects on the improvement of understanding, cheerfulness, calmness, and relaxation. Dosages of the drugs went as high as 100mg. It was thought that doctors who have heretofore hesitated using FE or FL in large quantities should try it out experimentally. 11 references.

000546 Hogarty, Gerald E. University of Pittsburgh, Pittsburgh, PA 15213 **Long-acting drugs with aftercare of schizophrenics.** Psychopharmacology Bulletin. 12(3):80-81, 1976.

A study is carried out to determine the differential effects of fluphenazine hydrochloride and fluphenazine decanoate on the tenus and adjustment of recently discharged schizophrenic patients receiving sociotherapy on an outpatient basis. The influence on relapse and adjustment patterns of insuring that patients receive medication (by supervised injection vs. oral self-administration) is being assessed. After discharge from the hospital (after treatment with oral fluphenazine) patients are randomly assigned to one of four treatments: long-acting fluphenazine decanoate injections with or without major role therapy (MRT), or short acting fluphenazine hydrochloride tablets with or without MRT. Injections or dosage adjustments are made biweekly and clinical evaluations are performed periodically for 2 years. The results of the study are in the interpretation stage.

000547 Ipar, Omar J.; Lozano, Luis O.; Romi, Juan Carlos; Morinelli, Julio Alberto; Cavadini, Ricardo Mario; Timbaldi, Alberto. Facultad de Medicina de la Universidad Nacional de Buenos Aires, Argentina **/Clinical study and evaluation of a new derivative of phenothiazine./** Investigacion clinica y evaluacion de un nuevo derivado fenotiacinico. Neuropsiquiatria (Buenos Aires). 6(2-3):139-145, 1975.

The clinical effectiveness of Methophenazine, when administered under various circumstances was evaluated. Oral administration to 60 adult patients in dosages of 5 to 25mg twice daily from one to six months was followed by a period of followup therapy with reduced dosages. Fifty three of the patients were schizophrenic; improvement was evaluated as nil, slight, or significant for twelve symptoms, ranging from psychotic anxiety to hyperactivity, in eight of which some degree of improvement was shown. Rehabilitative effects were similarly evaluated for 11 parameters ranging from quality of work to decision-making, in each of which improvement was shown, demonstrating the drug's excellent resocialization properties. The drug was generally tolerated well though some secondary effects were noted including moderate ataxia and some dyskinesia with spasmodic attacks. It is concluded that methophenazine is especially effective in long-term therapy toward the improvement of social contact and interpersonal relationships since it combats introversion and stimulates initiative. 11 references.

000548 Kiczak, Janina; Sliwinska-Przyjemska, Halina; Warnecka-Przybylska, Maria; Wdowiak, Maria Wanda. Klinika Psychiatryczna PAM, ul. Broniewskiego 1, 71-460 Szczecin, Poland **/Changes in serum enzyme levels during treatment with neuroleptics and thymoleptics./** Zachowanie sie nicktorych enzymow surowicy krwi podczas leczenia neuroleptykami i tymoleptykami. Psychiatria Polska (Warszawa). 10(2):153-158, 1976.

Serum enzyme levels were analyzed in a group of 55 schizophrenics (mostly paranoid) and 45 depressives (30 endogenous and 15 organic); the group consisted of 62 women and 38 men, 18 years to 58 years of age. The following drugs were administered: thiotixenes (Orloinamon, Navane), fluphenazine decanoate (Modliten-Depo), dibenzoazepine (Noveril-80 and Noveril-40) and doxepine (Sinequan). The levels of activity of the enzymes ChE, ALAT, AspAT and AP were determined before treatment, during maximum dosage and during sustained dosage. Results show that psychotropic drugs sometimes cause an increase in the indicator enzyme's activities (especially ALAT), while the activities of ChE and AP do not deviate from the norm. These changes are more common with neuroleptics than with thymoleptics. 12 references. (Author abstract modified)

000549 Klein, Donald F. Long Island Jewish-Hillside Medical Center, Glen Oaks, NY **Drug in the aftercare treatment of schizophrenia.** Psychopharmacology Bulletin. 12(3):81, 1976.

The prophylactic efficacy of injected fluphenazine decanoate (FD) vs. oral fluphenazine hydrochloride (FPZ) vs. placebo in schizophrenic patients receiving supportive therapy in an aftercare setting was investigated. The proportion of relapses during a 12 month study was two patients of 24 for FD, three patients of 27 for FPZ, and 14 patients of 22 for placebo. Eleven patients were terminated from the study because of side-effects: one patient because of oversedation, another patient because of dyskinesia and nine patients because of akinesia. Eight of the nine patients with akinesia had received FD. Complete or partial improvement in the patients terminated because of toxicity was achieved when they were shifted to a procyclidine regimen. The number of acute schizophrenics studied was too small to permit conclusions about the value of prophylactic medication for this diagnostic group. No clear trends emerged to indicate that acute schizophrenics or chronic schizophrenics are more prone to relapse or to toxic effects of fluphenazine.

000550 Klerman, Gerald L. Massachusetts General Hospital, Boston, MA **NIMH-PRB collaborative study of long-acting fluphenazine.** Psychopharmacology Bulletin. 12(3):81-82, 1976.

An comparison of a treatment regimen involving injections of long-acting fluphenazine decanoate with a regimen involving oral administration of fluphenazine hydrochloride is conducted in schizophrenics in order to determine: 1) whether relapse and rehospitalization are related to discontinuation of medication; 2) relief of symptoms by each regimen; 3) the effectiveness of each regimen in averting reemergence of symptoms; and 4) cost of treatment in terms of need for continuing inter-

vention and support by mental health and other community institutions. Particular attention is paid to rehospitalization patterns and patient functioning, including patient productivity and use of various community resources. Patients are interviewed and rated on a regular basis. Initial results of this project are forthcoming.

000551 Kondo, Hisao; Imai, Hidehiko; Takahashi, Saburo; Kato, Nobukatsu; Otani, Wataru; Department of Psychiatry and Neurology, Kyoto Prefectural University of Medicine, Kyoto, Japan **A double-blind controlled comparison of penfluridol and carpipramine on schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(11):1373-1386, 1975.

The effects of penfluridol and carpipramine were compared in a double-blind study on 86 (44 for carpipramine and 42 for penfluridol) schizophrenic patients on a fixed flexible schedule. The anti-Parkinson drug promethazine was administered in addition to either of the above. Overall improvement for the patients was 66.7% for penfluridol, and 34.1% for carpipramine. Penfluridol was superior in reducing excessive or abnormal movement and speech, reducing abnormalities in human relationships, improving attitudes toward others, and in work and recreational improvements. No difference in the side-effects could be noticed between the drugs. Among the side-effects noted were anxiety, and sensations of heat -- but these seemed to be less prevalent than for other tranquilizers. 5 references.

000552 Koshino, Yoshibumi; Matsumoto, Kanji; Otsuka, Ryosaku; Okishi, Keimei; Kawaai, Yoshiharu; Matsuoka, Munesato; Michishita, Chuzo. Department of Neuropsychiatry, Kanazawa University School of Medicine, Japan **A double blind comparison of TPN-12 and chlorpromazine on schizophrenia.** Medical Consultation & New Remedies (Tokyo). 12(9):2161-2173, 1975.

TPN-12 (3-methlsulphonyl-10-(2-N-methylpiperidyl-2)-ethyl-1)-phenothiazine) was compared to chlorpromazine in a double-blind study with 22 patients using TPN-12 and 21 using chlorpromazine (CPZ). The test was run for 8 weeks. Results were checked after the 1st, 4th and 8th week. No difference could be found in the effects of either drug on hallucinations and delusions, however, TPN-12 was inferior in treating emotional apathy. TPN-12 began taking effect after only 1 week, faster than CPZ. Dosage of TPN-12 was from 150-300mg/day and was considered to be about the same strength as CPZ in its effects. Side-effects of TPN-12 were the same as for other phenothiazine drugs, but seemed to occur more frequently. It is concluded that CPZ and TPN-12 and similar effects and were both equally good drugs for schizophrenia. 18 references.

000553 Lindholm, Halvar. Blackebergs Sjukhus, Sjukhemmet, S-16125 Bromma, Sweden **The consumption of inpatient psychiatric resources prior to and during treatment with a depot neuroleptic, perphenazine enanthate. A mirror study.** Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):513-520, 1975.

A mirror study to show the consumption of inpatient psychiatric treatment resources before and after treatment with perphenazine enanthate is described. Each patient functioned as his own control. The patients were given perphenazine enanthate (PE) at two mental hospitals on a depot basis. The trial group were 24 outpatients and inpatients with schizophrenia. The actual treatment period with PE was at least 1 year. A period of time immediately prior to therapy was established as the control period. Oral neuroleptics were prescribed for patients during at least 75% of the control period. The number of admissions per year and the number of treatment days per admission are less during the PE period compared with the control period. The results show significantly lower consumption of inpatient psychiatric resources during the PE period expressed as admissions per year and number of treatment days per admission. The registered reduction is also possibly due to the treatment program with PE and the possible influencing factors are discussed. 15 references.

000554 Luchins, Daniel. Allen Memorial Institute, 1025 Pine Avenue West, Montreal, Quebec, Canada **The dopamine hypothesis of schizophrenia: a critical analysis.** Neuropsychobiology (Basel). 1(6):365-378, 1975.

The evidence linking dopamine and schizophrenia is reviewed, surveying: studies on dopamine metabolites in schizophrenia: the effects of dopamine agonists, antagonists, and depletors on schizophrenia; and the action of present treatments of schizophrenia on dopamine. As well, interrelationship of dopaminergic, cholinergic, and gabanergic pathways is examined. It is concluded that the relationship between dopaminergic mechanisms and schizophrenia is nonspecific. The dopamine hypothesis is shown to reflect an attitude towards schizophrenia that emphasizes acute, florid symptoms. It is suggested that research directed towards studying dopaminergic mechanisms in specific psychopathological symptoms, not syndromes, might prove fruitful. 87 references. (Author abstract modified)

000555 Matsuoka, Masao. Osaka University, Japan **Amine metabolism.** In: Yokoi, S., Schizophrenia. Tokyo, Igaku Shoin, 1975. (p. 434-450).

Various research on the action of amines in metabolism is reviewed. Emphasis is placed on post-1950 research on amine metabolism and research into its relationship to schizophrenia and other mental illnesses. In particular, the work of Osmond and Hoffer on catecholamine and the effects of psychotominetic drugs on it are related. Similar research of other scientists (Armstrong, Friedhoff, Gaddum, Wolley) is also reported. Other research into protein, sugar, and nitrogen in metabolism is reviewed to indicate methods of determining a physical identifier or a blood toxin responsible for schizophrenia. Before this is found, more cooperation among biochemists, psychiatrists, neurochemists, and psychopharmacologists is deemed necessary. 71 references.

000556 Mattke, D. J.; Wisuschil, W. Max-Planck-Institut fur Psychiatrie, Deutsche Forschungsanstalt fur Psychiatrie, Kraepelinstr, 2 u. 10, D-8000 Munchen 40, Germany /**A method for studying pupillomotor effects of neuroleptics.**/ Eine Methode zur Untersuchung der Pupillomotorik unter dem Einfluss neuroleptischer Medikation. Arzneimittel-Forschung (Aulendorf). 26(5):946-950, 1976.

To investigate the pupillostatic effect of neuroleptics 40 schizophrenics, including 23 females and 17 males, 19 to 45 years old (average age 29), were given 1mg haloperidol or 10mg loxopin p.o. in a double-blind test and pupil diameter was measured daily on color photographis of the eye. A statistically significant change in pupil diameter was measured after the first dose of both drugs. The difference in pupillostatic effect paralleled the clinical findings that loxapine showed a more distinctly sedative effect that haloperidol. 16 references.

000557 Meltzer, Herbert Y. Dept. of Psychiatry, Univ. of Chicago Pritzker School of Medicine, 950 E. 59th St., Chicago, IL 60637 **Neuromuscular dysfunction in schizophrenia.** Schizophrenia Bulletin. 2(1):106-135, 1976.

Various causes of neuromuscular dysfunction are reviewed to evaluate theories on the etiology of the schizophrenic and affective psychoses. Dopamine is indicated as inhibiting skeletal muscle contraction by a direct effect on muscle which can be inhibited by chlorpromazine and haloperidol, suggesting there is a dopamine receptor in muscle. It is also noted that creatine phosphokinase (CPK) measurement in psychiatric patients may at times be of value for the differential diagnosis of nonpsychotic from psychotic patients. This review points toward evidence for an organic component of the major psychoses. It is possible that the causes of the neuromuscular dysfunction may be related to the causes of the psychoses themslves. 147 references.

000558 Meltzer, Herbert Y.; Stahl, Stephen M. Dept. of Psychiatry, U. of Chicago Pritzker School of Medicine, 950 E. 59th St., Chicago, IL 60627 **The dopamine hypothesis of schizophrenia: a review.** Schizophrenia Bulletin. 2(1):19-76, 1976.

The dopamine hypothesis described herein states that schizophrenia may be connected with a relative excess of dopamine (DA) dependent neuronal activity. This extensive review touches upon such topics as major dopamine tracts, retinal dopamine fibers, tuberoinfundibular dopamine system, incertohypothalamic dopamine tract, mesocortical DA system, mesolimbic DA system, synthetic pathways, regulation of dopamine synthesis and other neuronal activities, and dopamine storage, turnover and stress. Studies of dopamine synthesis and regulation in schizophrenia cover aspects of tyrosine hydroxylase inhibition, effects of L-dopa in schizophrenia, dopa decarboxylase inhibition, and decarboxylation of L-dopa by erythrocytes in schizophrenia. Other aspects mentioned are dopamine release and amphetamine psychosis, neuroleptics and the dopamine hypothesis of schizophrenia. Also briefly discussed are the following: the effects of drugs on dopamine and acetylcholine metabolism in striatal and limbic areas, presynaptic and postsynaptic effects of neuroleptics, the inactivation of dopamine by neuronal reuptake and enzymatic breakdown. Mentioned are dopamine metabolites in cerebrospinal fluid of schizophrenic patients, and dopamine in mania (following lysergic acid diethylamide), and in depression. 421 references.

000559 Narita, Shiro. Yotsuya Shinkei-ka, Japan **Clinical experience in using Penfluridol (TLP-607) for schizophrenia.** Medical Consultation & New Remedies (Tokyo). 12(7):1565-1591, 1975.

The effects of penfluridol (TLP-607) were tested on 51 inpatients and outpatients suffering from schizophrenia (delusional, pubescent, and tension schizophrenia). Overall effectiveness was rated at 69%. It was found especially effective against hallucinations, the delusional process, and rejection due to the influence of abnormal experiences. Sleepiness was noted in a few cases as a side-effect. Administration was oral, once or twice weekly. Since the quantity of this drug could be low while realizing maximum effect, it was concluded that administration of this drug was revolutionary in treatment for chronic schizophrenia. 12 references.

000560 Nava, V.; Drago, F. Ospedale Psichiatrico Provinciale di Como, Como, Italy **/Spontaneous assumptions of a pharmacotherapeutic role by two long-term schizophrenic patients./** Assunizione spontanea di un ruolo farmacoterapico de parte di due schizofrenici lougodegenti. Rassegna di Studi Psichiatrici (Siena). 65(2):365-370, 1976.

Clinical notes on two long-term institutionalized schizophrenic patients who spontaneously undertook psychopharmacologic therapy result in conclusions questioning the validity of some of the premises and institutional frameworks governing traditional institutionalized psychiatric treatment.

000561 Nishizono, Masahisa. Department of Psychiatry, Fukuoka University School of Medicine, Japan **Pharmacopsychotherapy of schizophrenia.** Japanese Journal of Psychotherapy. 1(2):134-143, 1975.

The inclusion of pharmacologic treatment in psychotherapy for types of schizophrenia where the cause is unclear is discussed. The history and the methods of treating schizophrenia are outlined and the four types of placebo reactions noted: apparent immediate improvement with instability; a stable but not pronounced improvement, deterioration of the condition; and no change in condition. Various drugs (chlorpromazine, butyrophenone, phenothiazine) and their effects are discussed. LSD treatment is evaluated as too unpredictable for practical use. Results of personal psychopharmacological experience are explained with regard to all phases of treatment. It is concluded that drug therapy is especially useful when root causes of the schizophrenia are unknown and regular phychoanalysis is ineffective. 29 references.

000562 Nishizono, Masahisa; Yonekura, Tomio; Toyonaga, Takemori; Sakaguchi, Nobutaka; Matsuguchi, Yoshinori. Department of Psychiatry and Neurology, Fukuoka University School of Medicine, Japan **Clinical effect of TPN-12 for schizophrenics -- compared with haloperidol by a double-blind test.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(6):689-709, 1975.

The clinical effect of TPN-12, an oxide of thioridazine (Melleril), on 60 schizophrenics was compared with that of haloperidol in a double-blind test. TPN-12 was given to 31 subjects and haloperidol to 29 subjects. Though not significantly different statistically, TPN-12 was either highly effective or showed significant improvement for response impediment to oral examination, inactiveness, hallucination, delusion and emotional disturbances. TPN-12 was also effective in behavioral improvement. Both groups showed a similar degree of side-effects in drowsiness, fatigue and autonomic nervous system disorders. TPN-12 group showed a higher degree of muscular side-effects of the extrapyramidal system and amenorrhea while the haloperidol group showed a higher degree of Parkinson's disease symptoms. Results suggest that TPN-12 is a safe antipsychotic drug which might be a little less effective than haloperidol. It is suggested for use on inpatients because of possible extrapyramidal symptoms. 19 references.

000563 Nomura, Shotaro; Sarai, Keisuke; Kodama, Hisashi; Ishizu, Hiroshi; Kubo, Setsuji; Kodama, Hidetoshi; Kawamura, Takahiro; Sasaki, Toshisuk. Department of Neuropsychiatry, Tottori University, Japan **Comparison of effects upon schizophrenia of methylperidol (Luvatren) by double blind examination and haloperidol.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(8):973-985, 1975.

A double-blind study was conducted to analyze the effectiveness of methylperidol and haloperidol in treating schizophrenics. Seventy two schizophrenic patients were divided into two groups; one group was administered 6mg of haloperidol per week and the other group 30mg of methylperiodol per week for 8 weeks. Results showed that 20 subjects in the methylperidol group and 23 in the haloperidol group improved; 12 in the methylperidol group and 8 in the

haloperidol group showed no results; negative results were produced in 3 in the methylperidol and 6 in the haloperidol group. A positive feature of methylperidol was its resultant, rapid, effectiveness in treating schizophrenics with emotional disorders and hallucination. There were fewer side-effects in the methylperidol group than in the haloperidol group, but both drugs caused sleep disorder suggesting a need for more research. 30 references.

000564 Rosengarten, Helen; Friedhoff, Arnold J. Millhauser Laboratories, N. Y. U. School of Medicine, 550 First Ave., N. Y., NY 10016 **A review of recent studies of the biosynthesis and excretion of hallucinogens formed by methylation of neurotransmitters or related substances.** Schizophrenia Bulletin. 2(1):90-105, 1976.

The biosynthesis and excretion of hallucinogens formed by methylation of neurotransmitters or related substances is discussed in terms of enzymatic formation. This indicates a major shift in emphasis away from the measurement of metabolites toward research on enzymes involved in biosynthesis. 110 references.

000565 Ruiz, Ruiz, M.; Miro Quintana, L.; Sentis Vilalta J. Escuela Profesional de Psiquitria de la Facultad de Medicina, Hospital militar del Generalisimo, Spain **/Clinical study of pimozide with chronic schizophrenics./** Estudio Clinico con pimocide en las esquizofrenias de evolucion cronica. Rev. de Psiquiatria y Psicologia Med. de Europa y America Lat. (Barcelona). 12(4):247-255, 1975.

A clinical study was made of the effect of pimozide on 40 patients having a history of schizophrenic symptomology for a year and a half or more. The study was conducted as follows; 1) maintenance for one month of same neuroleptical therapy previously used; 2) discontinuation of medication until symtoms reappeared; 3) renewal of previous treatment using optimal dosage for a 2 week period; 4) therapy with 6 to 12mg of pimozide; 5) double-blind study using pimozide and a placebo for a maximum period of three months. The statistical analyses comparing neuroleptics usually employed and pimozide shows the therapeutic superiority of the latter, and patients were able to adapt to family, work, and social life. 14 references. (Journal abstract modified)

000566 Sakurai, Masahiko; Takahashi, Ryo. Department of Psychiatry and Neurology, Nagasaki University School of Medicine, Japan **Metabolism of drugs in schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(2):189-196, 1975.

Important research findings relating to metabolism of chlorpromazine (CPZ) in the treatment of schizophrenics are presented. Discussion includes: 1) identification and pharmacological properties of metabolites of CPZ through urine analysis; 2) absorption, distribution, and excretion of CPZ; 3) CPZ concentration in the blood of the schizophrenic and the normal person; and 4) clinical effects of CPZ and its relationship to plasma level. 38 references.

000567 Selman, F. B.; McClure, R. F.; Helwig, H. Department of Psychiatry, University of Texas Health Science Center, Dallas, TX **Loxapine succinate: a double-blind comparison with haloperidol and placebo in acute schizophrenics.** Current Therapeutic Research. 19(6):645-652, 1976.

The clinical effectiveness and side effects of loxapine succinate, a tricyclic dibenzoxazepine derivative, were compared with the effectiveness and side effects of haloperidol and placebo during a 12 week double-blind study with 87 patients hospitalized with acute schizophrenia or acute exacerbation of chronic schizophrenia. The effectiveness of loxapine was comparable to that of haloperidol in reducing symptomatology on several rating scales, including the Nurses Observation Scale for Inpatient Evaluation and the Brief Psychiatric Rating Scale. The placebo group showed significant improvement at first, but results were not maintained and were significantly less than those of the active drugs at the end of the study. Side effects of the active drugs were comparable and more than those of the placebo. 5 references. (Author abstract modified)

000568 Shaskan, Edward G.; Becker, Robert E. Department of Psychiatry, University of Connecticut School of Medicine, Farmington, CT 06032 **Blood platelet monoamine activity in anergic schizophrenics.** In: Bernard, B., Aminergic hypotheses of behavior: reality or cliche? Rockville, MD, National Institute on Drug Abuse, 1975. 149 p. (p. 29-35).

Blood platelet monoamine oxidase (MAO) activity was evaluated in 24 anergic, schizophrenic outpatients during a double-blind study comparing a chlorpromazine/imipramine combination to thiothixene placebo. Platelet MAO activity was determined on blood samples drawn over a two week drug free washout and once weekly over a four week on drug period. Schizophrenic patients could be classified according to their blood platelet MAO activity into either a low MAO or a high MAO group. In neither group of this population of schizophrenics did blood platelet MAO activity correlate with any of the primary or secondary symptoms of schizophrenia. Ten alcoholics and seven volunteer nonpatients could similarly be divided into low and high MAO groups. Mean blood platelet MAO activity for these groups was not significantly different from the mean values of the low and high MAO groups of the schizophrenics. These findings do not support published reports of low blood platelet activity as a genetic marker for schizophrenia. Discriminate function analysis of symptomatology ratings at baseline was used to characterize the low and high MAO schizophrenic patient groups. Individuals in the low MAO group were distinguished by hyperactivity, anergia, and sleep disturbance. 16 references. (Author abstract)

000569 Shimizu, Junzaburo. Department of Psychiatry, National Konodai Hospital, Japan **Clinical experience in using TLP-607 for chronic schizophrenia.** Medical Consultation and New Remedies (Tokyo). 12(7):1593-1600, 1975.

Ten chronic female schizophrenics were orally administered TLP-607 for a period of 4 to 21 weeks. Three patients were given 80mg of TLP-607 biweekly and the seven others between 10 to 20mg per week, along with either neuroleptics, antihistamine, antiparkisonian drugs, or barbiturates. Four patients showed improvement, as they began to express feelings, gain self-confidence, and perform small tasks. Two patients discontinued the treatment due to severe insomnia and a loss of appetite, and four showed no improvement. Generally most of the patients had some side-effects such as insomnia and loss of appetite. 9 references.

000570 Takahashi, Saburo. Department of Psychiatry, Kyoto Prefectural University of Medicine, Japan **Schizophrenia and sleep disorders.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(9):1031-1038, 1975.

One important clue to a deteriarating stage of schizophrenia is a type of sleep disorder. The relationship between the hallucination and REM sleep compared with a normal person and

the effects of psychotropic drugs are discussed. Studies in REM sleep are also reviewed. The eeffect of REM sleep deprivation is noted using the examples of research conducted by Dement (1959), Zarcone (1969), and Azumi, Takahashi and Kikui (1967). It is believed that in reviewing the effect of chlorpromazine on the schizophrenia, there are two effective improvements in schizophrenic sleep disorders. It normalizes the decrease of deep sleep seen among schizophrenics, and it regulates REM sleep and REM action. Some literature indicates that lack of 5-hydroxytryptophan (5-HTP) would reduce the barrier between REM sleep and awakening. However, this is still hypothesis titical and no proof is shown. 41 references.

000571 Tansella, M.; Balestrieri, A. Institute di Clinica Psichiatrica di Verona, Policlinico di Borgo Roma, I-37100 Verona, Italy **The choice of neuroleptics in the treatment of schizophrenia: a critical review.** Arzneimittel-Forschung (Aulendorf). 26(5):943-945, 1976.

The selective use of different neuroleptics in the treatment of schizophrenia by some psychiatrists is discussed. Although many practitioners prescribe according to the patient's need for a sedative, antidelusional or activating effect, most extensive controlled studies have demonstrated no significant differences among neuroleptics in their therapeutic efficacy. The hypothesis that these drugs have specific and selective actions therefore cannot be accepted. For an individual patient, it seems more rational to choose the right dosage schedule rather than the right drug. Though the study of the metabolism of these drugs remains the most interesting approach to the problem of the individualization of therapy, the results of these studies have been disappointing in that plasma levels cannot consistently be correlated with clinical improvement. In clinical practice and important element in the process of selecting a neuroleptic is still the incidence of side effects. It is concluded that at this time the drug of choice can only be the drug best tolerated by the patient. 40 references. (Author abstract modified)

000572 Teja, Jagdish S.; Grey, William H.; Clum, Judith M.; Warren, Carmen. University of Va. School of Medicine, Charlottesville, VA 22901 **Tranquilizers or anti-depressants for chronic schizophrenics: a long term study.** Australian and New Zealand Journal of Psychiatry (Carlton). 9(4):241-247, 1975.

The efficacy of four tranquilizers (chlorpromazine, trifluoperazine, thiothixene, and haloperidol) and an antidepressant (amitriptyline) in the treatment of chronic schizophrenia was studied. Subjects were 66 patients hospitalized an average of 10 years, and medications were administered in a double-blind format. Following a 4 week placebo period, high dosages of the tranquilizers were given for 16 weeks, and amitriptyline was added for the next 16 weeks. Statistical analysis of the various change measures revealed that patients worsened significantly on placebo, all four tranquilizers were significantly better than placebo for symptom reduction, and maximum improvement was attained within 16 weeks of tranquilizer administration. No significant difference in efficacy was observed among the four tranquilizers, and addition of amitriptyline did not confer any additional therapeutic advantage. 22 references. (Author abstract modified).

000573 van Praag, H. M. no address **On the origin of schizophrenic psychoses.** Amsterdam, De Erven Bohn BV, 1975. 230 p.

The etiology, diagnosis, psychopharmacology, and genetics of schizophrenia are discussed, citing contributions from a number of European laboratories. Chapters of the book are devoted to the dopamine theory of schizophrenia; social analysis of schizophrenia; culture and schizophrenia; and the interconnections of dopaminergic, sertonergic, and noradrenergic pathways in the brain.

000574 Wojdyslawska, Irena; Siuchninska, Helena; Goraj, Andrzej. ul. Narutowicza 111, 90-154 Lodz, Poland /**Results of Leponex treatment in schizophrenia.**/ Wyniki leczenia Leponeksem chorych na schizofrenie. Psychiatria Polska (Warszawa). 9(1):45-50, 1975.

A group of 41 schizophrenic patients (25 females and 16 males, average age 33 years), mostly paranoid, were treated with Leponex (clozapine) for an average period of 57 days in doses ranging from 200-500mg/day for females and 300-650mg/day for males. Favorable results were obtained in 79% of the cases. The drug was particularly effective in cases with severe psychopathological symptoms, psychomotor hyperactivity, and manic tendencies. Leponex is a more powerful antipsychotic than other neuroleptics and is especially effective against delusions, hallucinations, anxieties, incoherence, aggression, and negativism. It also reduces autism and compulsive behavior. The most common side-effects were elevated body temperature (particularly in women), excessive salivation, tachycardia, and lowered blood pressure, but rarely with orthostatic collapse. 15 references.

000575 Wolf, Stewart; Berle, Beatrice Bishop. Harvard Medical School, Boston, MA **The biology of the schizophrenic process.** Advances in Behavioral Biology. Vol. 19. New York, Plenum, 1975. 199 p. $19.50.

Discussion conducted at the Totts Gap, PA, Colloquium on the Biology of Schizophrenia, May, 1975 is presented. The history of the evolution of the schizophrenic concept was traced, and evidence was presented for genetic transmission of at least one major form of schizophrenia. Studies of brain biochemistry, especially as reflected in pharmacologic data from psychotropic/therapeutic agents on the one hand and from pharmacologic stimulators of schizophrenia syndromes on the other, revealed information on the disorder. The role of life experience and environmental forces in the pathogenesis of schizophrenia was discussed, including controversial findings from monozygotic twins. Other potential factors in the disease included CNS involvement, such as birth trauma, minimal brain damage, infections, and other physiological stresses. Immunologic mechanisms and slow viruses were also suggested to explain the penetrance of a schizophrenic genetic trait.

000576 Wyatt, Richard Jed; Murphy, Dennis L. Clinical Psychopharmacology Lab., NIMH, St. Elizabeths Hosp., WAW Bldg., Wash., DC 20032 **Low platelet monoamine oxidase activity and schizophrenia.** Schizophrenia Bulletin. 2(1):77-89, 1976.

The potential significance of low blood platelet monamine oxidase (MAO) activity in schizophrenic patients is examined in relation to biologic factors related to psychiatric disorders. Early studies indicated that chlorpromazine had some inhibitory effect on MAO activity; but recent clinical tests with neuroleptics indicate no consistent differences in platelet MAO activity. The investigation suggests that this enzyme activity should be measured in other regions of the body such as kidneys, muscles, liver and lungs and results compared with measurements in the brain. 32 references.

000577 Yamada. Hiroaki. Department of Psychiatry, Kokufuzu Hospital, Odawara, Japan **Clinical experience of thiothixene (Navane) for schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(5):577-583, 1975.

Thiohixene (Navane), which combines the antidepressant effect of chlorprothixene and the mental invigorating effect of thioproperazine, has been reported effective in treating hallucinations and delusions of schizophrenic patients. This result was retested with a group of 30 schizophrenic patients. Results of the administration and the period of administration are charted for all 30 patients with changes in their symptoms. It was found very effective in 8 cases, effective in 16, and ineffective in 6 of the cases. There was a large difference in the effective dosage, but it was between 20 and 120mg.,averaging 30-40mg. Improvement usually resulted within 3 to 4 weeks of treatment, shortly after the appearance of any side-effects. It had a tranquilizing as well as an antihallucinatory effect. No adverse withdrawal reactions were noted. 9 references.

000578 Yamanoue, Sakae. Department of Neuropsychiatry, Osaka Municipal University School of Medicine, Japan **Clinical effect of Penfluridol for schizophrenia -- especially delusion.** Medical Consultation & New Remedies (Tokyo). 13(1):117-130, 1976.

Penfluridol (Easer) was tested on 21 schizophrenic patients (10 male, 11 female) between the ages of 17 and 53 to determine its effects. After 16 weeks of treatment, patients showed an overall 50% rate of improvement with the drug: very effective on two, effective on five, slightly effective on five, no change in six, and change for the worse in three cases. It was effective mostly in controlling overexcitation, strange movements, delusions, hallucinations, and other impairments of self-consciouness. It was between 20 and 30% effective for sensual, emotional, and speech impediments. Maximum effect of the drug was noted after 6 weeks of use. Fifteen of the subjects experienced side-effects of such as Parkinson's symptoms, menstrual irregularities, constipation, worry, pain and insomnia. Administration of the drug once per week was found sufficient, with administration 2-3 times per week causing a marked increase in side-effects. 18 references.

000579 Zahn, Theodore P. Laboratory of Psychology and Psychopathology, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **On the bimodality of the distribution of electrodermal orienting responses in schizophrenic patients.** Journal of Nervous and Mental Disease. 162(3):195-199, 1976.

Data are presented from four studies on the electrodermal orienting response (OR) in drug free schizophrenics which fail to confirm the findings of Gruzelier and Venables of a markedly bimodal distribution of ORs in schizophrenic populations. A review of the findings of other earlier studies, none of which confirm the bimodal hypothesis although some used patients taking phenothiazines, shows that differential effects of drugs, although probably an important factor, by itself cannot account entirely for the discrepancies in results. It is hypothesized that due to changes in hospital discharge policies, the groups of patients tested by Gruzelier and Venables, compared to those tested in earlier studies, were more heavily weighted with patients whose symptoms were resistant to phenothiazines. These patients may either have come from the extremes of the responsivity distribution or have atypical reactions to neuroleptic drugs. 14 references. (Author abstract)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

000580 Abuzzahab, F. S., Sr.; Dahlman, H. C.; Zimmermann, R. L. Dept. of Psychiatry, University of Minnesota, Minneapolis, MN 55455 **A three year double blind investigation of the effects of lithium carbonate on serum protein-bound iodine in manic depressive patients.** Neuropsychobiology (Basel). 1(5):304-312, 1975.

In a controlled investigation of the long-term effect of lithium on protein bound iodine (PBI), 17 manic-depressive patients were placed on lithium for 6 months then shifted on a double-blind basis to lithium (eight patients) and placebo (nine patients), and followed for a maximum of 3 years. Serum PBIs and lithium levels were evaluated initially and every 3 months thereafter. The placebo group showed no significant change in PBI during the first 6 months while still on lithium. At 9 months and 12 months evaluations, a rise in serum PBI was noted. Seven placebo patients with data available displayed a mean 6 month PBI of 6.26 plus or minus 0.67 microgram and at 9 months 7.07 plus or minus 0.63 micrograms. Available data for seven placebo patients at 6 months and 12 months show means of 6.30 plus or minus 0.66 micrograms and 7.06 plus or minus 0.56 micrograms, respectively. Patients on lithium during the entire study had a PBI of 6.95 plus or minus 0.81 micrograms at 6 months, which dropped to 5.76 plus or minus 0.36 micrograms after an average of 810 days of treatment. The placebo group showed no statistically significant change in PBI. 19 references. (Author abstract)

000581 Asano, Kaku; Satomi, Ryuta; Fujieda, Toshiyoshi; Ueno, Takeji; Suzuki, Nobuhiro; Mori, Yoshiomi; Fakatsu, Ryo; Okada, Fumihiko; Yamashita, Kaku. Department of Neuropsychiatry, Hokkaido University, Japan **Blood serum densities of tricylic antidepressants -- views gained through theraputic use.** Psychiatria et Neurologia Japonica (Tokyo). 77(10):746-747, 1975.

Blood serum measurements of tricyclic antidepressant drugs imipramine and amitriptyline were measured in depressed patients with a gas chromatograph. A report (results not quoted) was made about these measurements during treatment. Problems left to be resolved by the test were the conditional biologic changes caused, and effects of using two or more drugs simultaneously on the blood serum densities.

000582 Baron, D. P.; Unger, H. R.; Williams, H. E.; Knight, R. G. Sunnyside Hospital, Christchurch, New Zealnad **A double blind study of the antidepressants dibenzepin (Noveril) and amitriptyline.** New Zealand Medical Journal (Dunedin). 83(562):273-274, 1976.

A study was performed to compare the efficacy of dibenzepin and amitriptyline in the treatment of endogenous depression. Both drugs appear to be equally effective in the treatment of depression, but dibenzepin was more efficient in reducing associated anxiety. Both drugs are appropriate to the treatment of psychotic depression and work equally rapidly. Dibenzepin appears to elicit less intense side-effects. 12 references. (Author abstract modified)

000583 Bennie, Ernest H. Leverndale Hospital, Glasgow, Scotland **Depot neuroleptics.** British Medical Journal (London). No.6022:1404, 1976.

Reports on the use of depot neuroleptics in pharmacological management of chronic schizophrenia and other conditions, including nonpsychotic states, are presented. Successful treatment was of nonpsychotic patients with depot neuroleptics in-

cluding severe behavioral disorders, aggressive psychopathy, and alcoholism. A heterogeneous group of eight resistant neurotic patients were given fluspirilene in a dose ranging from 2 to 4mg/week. This type of intramuscular therapy has been successful in resolving symptoms where previous oral therapy with antidepressant drugs and benzodiazepines had not been successful. Responsive patients presented with paranoid, depressive, or phobic symptoms associated with behavioral irritability. Patients whose symptoms were entirely subjective did not respond to fluspirilene. It is suggested also that intramuscular administration of tranquilizers has advantages over the oral route. 2 references.

000584 Bunney, W. E., Jr.; Murphy, D. L. Adult Psychiatry Branch, and Laboratory of Clinical Science, DCBR, NIMH, Bethesda, MD 20014 **Neurobiological considerations on the mode of action of lithium carbonate in the treatment of affective disorsers?** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(3):142-147, 1976.

The effects of lithium on membrane function and cellular processes are considered in relation to lithium's physicochemical properties. Several cellular regulatory functions, including cyclic AMP formation and metabolism and biogenic amine neurotransmitter metabolism, are examined as possible mechanisms whereby lithium might exert its mood stabilizing actions. The necessity for understanding lithium's interactions with receptors, (the molecular sites affected by lithium,) in considering its presynaptic and postsynaptic effects is emphasized. 41 references. (Author abstract)

000585 Christiansen, C.; Baastrup, P. C.; Transbol, I. Department of Clinical Chemistry, Glostrup Hospital, 2600 Glostrup, Denmark **Osteopenia and dysregulation of divalent cations in lithium-treated patients.** Neuropsychobiology (Basel). 1(6):344-354, 1975.

The bone mineral content (BMC) in both forearms (highly correlated to total body calcium) was measured by photon absorptiometry in a representative sample of manic depressive patients receiving lithium treatment. The mean BMC values were 93% of normal, and the mean increases in serum levels of calcium and magnesium were 2mg/l. The incidences of osteopenia, hypercalcaemia, and hypermagnesaemia were 16%, 12%, and 30%, respectively. These results indicate that lithium treated manic-depressive patients have a disturbance in the mineral metabolism, be it due to the disease or the treatment given. 31 references. (Author abstract)

000586 Cole, E. N.; Link, Janet; Groom, G. V.; O'Flanagan, P. M.; Seldrup, J. Tenovus Institute for Cancer Research, Cardiff, Wales **Plasma prolactin concentrations in patients on clomipramine.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):93-100, 1976.

Human prolactin in plasma from depressed patients treated with clomipramine were estimated by radioimmunoassay. It is observed that some psychoactive drugs affect the secretion of prolactin from the pituitary, and that some of the many actions of prolactin itself could relate to mental illness as well as to breast cancer and reproductive physiology. In patients undergoing clomipramine therapy, plasma prolactin concentrations rose within 1 hr of drug infusion, and preinfusion levels rose progressively during the course of treatment over one week. Although Hamilton ratings showed a decline while prolactin rose, no correlation between mental illness and prolactin could be found for individual patients. Pretreatment values were within the range found for the normal population. Comment on these observations is included, focusing on possible testicular damage caused by high dosage clomipramine treatment, several natural disturbances of prolactin secretion, such as in idiopathic galactorrhoea, prolactin activity during pregnancy during lactation, and the effects of reserpine treatment on prolactin levels. 25 references. (Author abstract modified)

000587 Coper, H.; Fahndrich, E.; Rosenberg, L. Institut fur Neuropsychopharmakologie der Freien Universitat Berlin, Ulmenallee 30, 1 Berlin 19, West Germany **The rate of excretion of VMA in depressed patients before and after the administration of methionine.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 8(5):318-321, 1975.

The results of a previous experiment in which the relationship between VMA excretion in the 24 hour urine and a depressive syndrome was found, were examined in the present study on the basis of the following hypotheses: 1) patients of the present study showed an increased VMA excretion because there were more depressed patients than in the previous experiment; 2) the amount of excreted VMA correlates positively with the degree of severity of the depressive symptoms. The mean value of the VMA excretion in the urine of 20 depressive patients in the present study corresponds to that obtained from the depressive patients in the previous exploratory study. The degree of severity of depression of the patients corresponded positively with VMA excretion. Patients with increased VMA excretion were significantly more frequently treated with antidepressants than those with normal VMA values. 5 references. (Author abstract modified)

000588 Coppen, A. MRC Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **The effective dosage of antidepressants.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):72-74, 1976.

Research to establish effective dosage of antidepressants is briefly reviewed, emphasizing that numerous studies have shown that depressed patients treated with a standard dose reveal a wide range of blood plasma levels of the drug. It is argued therefore that the effective dosage must be found for each individual patient, either by monitoring blood levels or by other biological measures. Comment on these observations is included, focusing on a recent finding that deluded patients generally do not respond to treatment no matter what the blood levels of drug, as well the relationship between the pharmacological effects of drugs and their dose and/or plasma levels and methodological considerations in conducting plasma assays, measuring protein binding, and investigating enzyme induction variations. 8 references. (Author abstract modified)

000589 Coppen, A.; Gupta, R.; Montgomery, S.; Bailey, J. Medical Research Council Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **A double blind comparison of lithium carbonate and ludiomil in the prophylaxis of unipolar affective illness.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(3):94-99, 1976.

A double-blind prospective study compared the prophylactic effect of maprotiline (ludiomil) and lithium carbonate over a period of 1 year in patients suffering from recurrent affective disorders. The average Affective Morbidity Index was lower, but not significantly so, in patients treated with lithium. A further analysis based on dividing patients into those with no affective morbidity and those who showed some affective morbidity during the study, demonstrated lithium carbonate to be significantly superior to maprotiline in both the group as a whole and in unipolar depressives. 13 references. (Author abstract)

000590 Coppen, Alec; Montgomery, S. A.; Gupta, R. K.; Bailey, J. E. Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **A double-blind comparison of lithium carbonate and maprotiline in the prophylaxis of the affective disorders.** British Journal of Psychiatry (London). 128:479-485, 1976.

A double-blind prospective study was carried out comparing the prophylactic effect of maprotiline and lithium carbonate over a period of 1 year in patients suffering from recurrent affective disorders. The average Affective Morbidity Index was lower, but not significantly so, in patients treated with lithium. A futher analysis, based on dividing patients into those with no affective morbidity and those who showed some affective morbidity during the study, demonstrated lithium carbonate to be significantly superior to maprotiline both in the group as a whole and in unipolar depressives. A correlation between high plasma maprotiline concentration and low morbidity was observed. A highly significant negative correlation was found between plasma maprotiline concentration and body weight. Although the results show lithium carbonate to be superior to maprotiline, it should be emphasized that the plasma levels of lithium were constanly monitored and maintained at what is considered to be its optimum concentration, whereas the maprotiline treated patients were kept on a fixed dosage regime irrespective of plasma levels. It is suggested that maprotiline should be prescribed in doses related to body weight to achieve optimum blood levels of the drug. A dose of 3mg per kilogram of body weight is recommended. 16 references. (Author abstract modified)

000591 Corona, G. L.; Fenoglio, L.; Pinelli, P.; Zerbi, F. Clinica delle Malattie Nervose e Mentali, Facolta di Medicina e Chirurgia, Universita di Pavia, Pavia, Italy **/Mode of action of amitriptyline in depression: conceptual premises and criteria for evaluation./** Sulla modalita d'azione dell'amitriptilina nei depressi: premesse concettuali e criteri di valutazione. Archivio di Psicologia, Neurologia e Psichiatria (Milano). 36(4):493-504, 1975.

The efficacy of amitriptyline in depressive staes was clinically tested. The subjects were: 18 neurotic depressives, receiving 50mg/day; 21 neurotic depressives receiving placebo; 9 neurotic depressives receiving 100mg/day; 15 involutive depressives receiving 50mg/day; and 16 unipolar depressives receiving 150mg/day. Results were evaluated with the Hamilton and Braithwaite tests, taking side-effects into consideration. Improvements in the various patient groups are discussed from the viewpoint of possible existence of a critical effective dose of amitriptyline. The definition of endogenous and neurotic depression, drug response and drug plasma level, and the concept of cerebral shift are analyzed. 42 references.

000592 Davidson, Jonathan R. T.; McLeod, Malcolm N.; White, Helen L.; Raft, David. John Umstead Hospital, Butner, NC 27509 **Red blood cell catechol O-methyltransferase and response to imipramine in unipolar depressive women.** American Journal of Psychiatry. 133(8):952-955, 1976.

The response to imipramine was investigated by measuring baseline red blood cell catechol O-methyltransferase (COMT) in 15 unipolar depressive women. A linear correlation between COMT and response to imipramine (best outcome occurring at low COMT) was found. The results of this study were not related to such variables as intensity of depression, family history, or psychiatric history. It is suggested that this assay may be useful either as a predictor of response to the drug or as a guide in choosing the optimum dose. 28 references. (Author abstract modified)

000593 Davies, Brian; Burrows, Graham; Scoggins, Bruce. Dept. of Psychiatry, Clinical Sciences Building, Royal Melbourne Hospital, Victoria 3050, Australia **Plasma nortriptyline and clinical response.** Australian and New Zealand Journal of Psychiatry (Carlton). 9(4):249-253, 1975.

Twenty two depressive patients were treated with various doses of nortriptyline to determine whether the resulting plasma levels could be related to changes in the severity of the depression. Significant correlations with changes in depression were not shown in Hamilton Depression Scores. Cases of individual patients who have been known to respond to the chemical action of the drug as indicated by serum level are cited. It is suggested that response by group is difficult to show because of the tendency to spontaneous recovery and the variations in plasma levels in patients given the same oral dosage. 6 references.

000594 Dorr, C.; Sathananthan, K. Department of Metabolic Research, Warlingham Park Hospital, Warlingham, Surrey, England **Treatment of mania with bromocriptine.** British Medical Journal (London). No. 6021:1342-1343, 1976.

Pharmacokinetic principles are described with relation to drug trials with bromocriptine for the treatment of mania. Bromocriptine, a semisynthetic ergot alkaloid, semisynthetic ergot alkaloid, stimulates dopamine receptors in the nigrostriatum of the brain, lowers plasma prolactin levels, and has little direct effect on the uterus or cardiovascular system. It also acts presynaptically, possibly at pituitary level. Biochemical precursors of 4-hydroxy-3-methoxyphenylethylene glycol, found increased in the cerebrospinal fluid in mania, include prolactin produced by the pituitary gland. On these principles, lowering of plasma prolactin level with bromocriptine should prevent the genesis of mania without producing the side-effects associated with phenothiazines or potential toxic reactions associated with lithium. Treatment with bromocriptine was found psychosis who developed severe mania and in whom phenothiazines and lithium carbonate were contraindicated. Further evaluation of the drug is being carried out. 5 references.

000595 Dotti, Andrea. Universita degli Studi di Roma, Istituto di Psychiatria, Rome, Italy **/Five years' experience with lithium carbonate./** Cinque anni di esperienza con il carbonato di litio. Rivista di Psichiatria (Roma) 10(3):215-230, 1975.

A study was made of 149 patients with manic depressive psychosis treated with lithium carbonate for a period of 5 years. Patients included 69 males and 80 females between the ages of 19 and 72 years and all received 400mg/day lithium carbonate P.O. Results showed: 1) lithium carbonate prevented manic depressive reoccurences in a great number of patients; 2) manic seizures occured more often after therapy than in the depressive phase, but the latter responsded to drug therapy more rapidly and seizures were less serious; 3) a few months were sometimes necessary for observable effects; 4) seriously ill manic depressives did not respond very well to lithium carbonate drug therapy; 5) lithium exhibited low toxicity and affected thryoid and kidney functions in only a few cases. 16 references.

000596 Dunner, David L.; Fleiss, Joseph L.; Fieve, Ronald R. 722 W. 168th St., New York, NY 10032 **Lithium carbonate prophylaxis failure.** British Journal of Psychiatry (London). 129:40-44, 1976.

Data from non rapid cycling bipolar (manic-depressive) patients who were receiving long-term treatment with lithium

carbonate are analyzed by the life table method to determine when lithium carbonate prophylaxis failures occurred. Forty four of 96 patients failed to keep well in spite of maintenance lithium therapy. The analysis revealed an early, rapid failure rate during the first 6 months of treatment, which was followed by a slower rate of failure. Several clinical factors were assessed to determine if any of them predicted which patients would experience their initial failure in the early or late interval, but none of these factors, which included age, sex, age of onset, rate of affective attacks, family history, and the nature of the preceding episode, were found to have any predictive value regarding lithium prophylaxis failure. It was found, however, that patients who had early failures tended to have a subsequent early failure in spite of continued maintenance with lithium carbonate. 9 references. (Author abstract)

000597 Eckmann, F. no address **/Nootropic characteristics in psychoorganic senility syndrome exposed by the double-blind method./** Mise en evidence par la methode en double aveugle des proprietes des nootropes dans les sindromes psycho-organique seniles. Medicina Psicosomatica (Roma). 20(4):371, 1975.

Paranoid/depressive disorders of mood were discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Piracetam or placebo was given to 60 elderly patients in a randomized double-blind study. Results were recorded in the form of punched cards. Statistical evaluation showed that: 1) the favorable effect of piracetam on paranoid/depressive psychosyndrome of elderly patients was statistically significant; 2) comparison of the two treatments by binomial distribution showed that improvement under placebo was nonsignificant, compared to significant improvement under piracetem; 3) the onset of piracetam activity in the first 2 weeks of therapy was highly significant, and a positive effect continued until 14th day of treatment. (Author abstract modified)

000598 Elwan; Osamah; Taher, Yehra; Allam, Mahmoud; Hassan, Mahassen Aly. 30 Adly Street, Cairo, Egypt **A comparative study of antidepressants in the treatment of depressive states.** Journal of International Medical Research (Northampton). 4(3):202-210, 1976.

The effect of 6 antidepressive drugs of either (a) the tricyclic group (amitriptyline, dibenzepine, doxepin, noxiptyline) and tetracyclic group (maprotiline), or (b) MAO inhibitor group (nialamide), was investigated in 6 groups of patients, each consisting of 20 patients suffering from depressive states. The overall response of the 6 groups as well as the response of the individual target symptoms of depression according to the Hamilton Rating Scale were reported. These drugs can be classified into three groups: 1) antidepressants with predominant anxiolytic and sedative properties represented by amitriptyline and doxepin; the former has a superior mood elevating property while the latter possesses more anxiolytic and sedative effects; 2) antidepressants with predominant energizing and drive stimulating effects represented by dibenzepine and to a much lesser extent by nialamide; 3) antidepressants having an intermediate broad spectrum action producing both anxiolytic and energizing effects, represented by maprotiline and noxiptyline the former being more potent as an anxiolytic and the latter having a greater mood elevating property. 20 references. (Author abstract modified)

000599 Ende, W. Nervenklinik Hochweitzschen, DDR-7301 Westewitz uber Dobeln, Germany **/Long-term lithium therapy of geriatric manic-depressives./** Zur Lithiumdauermedikation bei manisch-depressiven Erkrankungen im hoheren Lebensalter. Zeitschrift fur Alternsforschung (Berlin). 30(4):351-357, 1975.

A review of clinical results in long-term lithium therapy of 57 geriatric patients with affective psychoses (manic-depressive) is presented. Lithium has proven to be an effective psychopharmaceutical agent in the treatment of geropsychiatric patients, even in view of the therapeutic complications encountered in the course of these disorders. Methods for reducing treatment risks to a minimum are outlined. 22 references. (Author abstract modified)

000600 Escobar, Javier I.; Teeter, Richard R.; Tuason, V. B.; Schiele, Burtrum C. St. Paul-Ramsey Hospital and Medical Center, St. Paul, MN 55101 **Intravenous chlorimipramine and depressive subtypes.** Diseases of the Nervous System. 37(6):325-328, 1976.

An open clinical trial with intravenous chlorimipramine was carried out on twenty depressed inpatients, diagnosed as primary or secondary affective disorders, following a classificatory scheme for use in psychiatric research. Eleven out of twelve patients with primary affective disorders had a significant decrease in symptoms of depression at the end of two weeks. In contrast, eight patients with secondary affective disorders did not show such significant improvement. Changes in physiological parameters (systolic blood pressure) were significantly greater in the primary affective disorders than in the secondary ones. It is inferred from the results of this trial, that intravenous administration of chlorimipramine is safe and feasible procedure, which may compare to electroconvulsive therapy in the treatment of severe unipolar and bipolar depressions. 19 references. (Author abstract)

000601 Fieve, R. R.; Dunner, D. L.; Kumbaraci, T.; Stallone, F. New York State Psychiatric Institute, Lithium Clinic, New York, NY **Lithium carbonate prophylaxis of depression in three subtypes of primary affective disorder.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(3):100-107, 1976.

Multiple indices of depression were used to evaluate the prophylactic efficacy of lithium carbonate versus placebo in a 4 year, double-blind study of unipolar, bipolar I, and bipolar II depressive patients diagnosed according to strict criteria. Data indicate lithium prophylaxis of depression on several indices in all three subtypes of affective illness. Additional studies are needed, comparing tricyclic antidepressants alone, monoamine oxidase inhibitors alone, or either drug in combination with lithium carbonate for prophylaxis in clearly defined depressive subtypes. 32 references. (Author abstract)

000602 Fieve, Ronald R. no address **Moodswing: the third revolution in psychiatry.** New York, William Morrow, 1975. 280 p. $8.95.

Management of manic-depressive illness with lithium is discussed, and the operation of a lithium clinic is described. The potential use of lithium in the long-term reduction of agressive behavior, certain forms of alcoholism, some phobias, obsessive/compulsive anxiety states, emotional disorders of children and adolescents and recurrent menstrual depression is suggested. Consideration is also given to the misdiagnosis of forms of manic-depression which masquerade as other disorders; psychiatric intervention in government and politics to control behavior based on affective disturbances; and the efficacy of psychotherapy in bipolar depressions.

000603 Fieve, Ronald R.; Kumbaraci, Turkan; Dunner, David L. New York State Psychiatric Insitute, 722 West 168th Street, New York, NY 10032 **Lithium prophylaxis of depression in bipolar I, bipolar II, and unipolar patients.** American Journal of Psychiatry. 133(8):925-929, 1976.

Lithium prophylaxis of depression in bipolar I (N=35), bipolar II (N=18), and unipolar I (N=28) outpatients was investigated. Depression indices included frequency of depressive episodes, three measures of severity, dropouts due to depression, and time in study. There were significantly fewer episodes and dropouts due to depression in the lithium treated than in the placebo treated bipolar I patients. Lithium was superior to placebo on all indices in the bipolar II group (although the sample size did not permit statistical analysis) and on three indices in the unipolar group. It is concluded that lithium prophylaxis of depression has been demonstrated in these three subtypes but the need for further research, particularly in the use of tricyclic antidepressants is emphasized. 25 references. (Author abstract modified)

000604 Francesconi, G.; Lo Cascio, A.; Mellina, S.; Fici, F.; Bagnoli, M.; Lepore, R. S. Maria della Pieta Psychiatric Hospital, Rome, Italy **Controlled comparison of melitracen and amitriptyline in depressed patients.** Current Therapeutic Research. 20(4):529-540, 1976.

Results of a comparison of melitracen with amitriptyline in a double-blind clinical trial with 30 hospitalized patients are summarized. Comparison between mean scores on the Hamilton Rating Scale for Depression and the Symptoms Check List showed no statistically significant difference between melitracen and amitriptyline. Examination of individual items of the Hamilton Scale, however, showed that melitracen modifies more rapidly and with greater intensity some important symptoms of the depressive state. Melitracen in comparison with amitriptyline has a more marked and more rapid antidepressant and disinhibiting activity. Side-effects in the melitracen group of patients were qualitatively similar to those of amitriptyline groups, but less intense and less frequent. Results confirm the efficacy of melitracen in the treatment of endogenous depressions. It appears particularly useful for treatment of depressive syndrome in outpatients who require well tolerated drugs with rapid action. 40 references. (Journal abstract modified)

000605 Franco, J.; Rendueles, G.; Noguera R. Hospital Psiquiatrico de Salt, Gerona, Spain **/Contribution of slow release neuroleptics on opening up the mental hospital./** La contribucion de los neurolepticos retard a la apertura del hospital psiquiatrico. Rev. de Psiquiatria y Psicologia Med. de Europa y America Lat. (Barcelona). 12(4):238-245, 1975.

Twenty chronic psychotic patients are discussed who underwent treatment with Eutimox designed to keep them hospitalized for as short a time as possible. The experiment showed the advantages of slow release neuroleptics in terms of shortening the period hospitalization in saving of material and time. Moreover, after release from the hospital, family can administer the medication to the patient. 12 references. (Journal abstract modified)

000606 Freyhan, F. A. 2015 R Street, N.W., Washington, DC 20009 **How long should prophylactics be continued in affective disorders?** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(3):137-141, 1976.

The contrasting modalities of phase directed therapeutic management and prophylactic drug treatment of affective disorders is traced historically in order to evaluate the proper duration of prophylactic treatment for individual illness profiles. An early treatment program testing compensatory drug treatment feasibility at Delaware State Hospital illustrates early states of treatment by imipramine or neuroleptics on 5 to 10 year tricyclic antidepressant regimes until lithium treatment was introduced. Lithium's stabilization of pathological mood swings is credited with advancing the concept and administration of prophylactic treatment of affective disorders, and the clinical course of recurrent manic-depressive illness. It is suggested that prophylactic treatment of affective illness should not automatically continue indefinitely but should depend on the individual case prognosis. 10 references.

000607 Friedman, Alfred S. Philadelphia Psychiatric Center, Philadelphia, PA **Drug and family therapy in depressed outpatients.** Psychopharmacology Bulletin. 12(3):82-83, 1976.

The effects of amitriptyline, alone and in combination with marital therapy and family oriented therapy, psychotherapy alone, or placebo and minimal individual patient-doctor contact were evaluated in depressed outpatients. Both the active drug and the marital therapy treatment conditions were superior to control conditions in treating depression. Drug effects were more pronounced and faster than those of marital therapy for symptom relief and clinical improvement. Marital therapy effects were superior to active drug effects on patients' self-ratings of performance in family role tasks and on patients' ratings of spouses' behavior in the marital relationship. For reducing hostility and enhancing perception of the marital relationship, drug therapy had a better early effect, but marital therapy had superior effects by the end of 12 weeks of treatment. Patients receiving placebo along with minimal physician contact showed greater improvement than has been reported in the majority of controlled drug studies with depressed outpatients.

000608 Fujiwara, Jiro; Baba, Osamu; Otsuki, Saburo. Department of Neuro-psychiatry, Okayama University School of Medicine, Okayama, Japan **Effects of flupenthixol in counteracting depressive states.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(4):447-452, 1975.

To study the effects of flupenthixol in counteracting depressive states, 24 depressive patients were administered 1-3mg of flupenthixol per day. Results indicated: four cases were remarkably improved, four improved, seven somewhat improved, and nine showed no improvement. Rapid improvement was generally observed within a week. Side-effects were found in nine patients with the most common depressives who responded poorly to psychotropic drugs. 9 references.

000609 Furlan, P. M.; Battaggia, P. G. Clinica delle Malattie del Sistema Nervoso della Universita di Torino, Turin, Italy **/Psychodynamic evaluation of a case of autoerotic fetishism./** Valutazione psicodinamica di un caso di feticismo autoerotico. Rivista di Patologia Nervosa e Mentale (Firenze). 96(5):287-300, 1975.

A case of fetishism, whose principal features were the homosexual or autoerotic choice of hair as the fetish, social and occupational maladjustment and occurrence of psychotic depression, is presented. Subject was a 22-year-old male who had spent many years in an orphanage, was abandoned by his mother, and never knew his father. He always felt the family nucleus was lacking in his life and considered himself a stranger, even to close relatives. At 12 years of age he was seduced by an adult and forced to perform homosexual acts. At 15 years of age he also had homosexual relations with some

school friends and it was then that he developed an intense curiosity about hair, givin rise to his fetish. Analysis of this case suggests that severe structural gaps in the subject's personality, and weakness of functioning of the Id mechanism, may be traced to the many serious and prolonged disturbances in his life, such as the absence of the father figure, instability of the mother, and long periods of institutionalization. Antidepressant and anxiolytic drugs were administered and frequent interviews were used to assist in recovery. Only after his depression showed signs of some amelioration was it possible to see any progress. It is concluded that this case could not be classified as a typical one of fetishism, narcissistic disturbance of personality, or psychoses, due to its particular features. 27 references.

000610 Gifford, L. A. Department of Clinical Pharmacology, St. Bartholomew's Hospital, London, England **Progress towards a comprehensive plasma assay for the tricyclic and tetracyclic antidepressants.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):69-71, 1976.

Advance in developing a comprehensive plasma assay for the tricyclic and tetracyclic antidepressants are briefly reviewed, emphasizing that accurate dose/response data for psychotropic drugs are difficult to obtain because of the lack of reliable criteria for measuring their effects. Studies of the relationship between the pharmacokinetics and the pharmacological effects of these drugs are therefore considered sidered particularly important. Recent advances in analytic techniques, especially the development of highly specific gas chromatography approaches which use alkali thermal ionization detectors, are enabling development of routine assay procedures capable of measuring therapeutic levels of all the tricyclic and tetracyclic antidepressants in common use. Comment on these observations in included, focusing on the stage at which the internal standard is added in the new chromatographic instruments and the column temperature which is used. 9 references. (Author abstract modified)

000611 Gisselmann, A. no address **/Use of lithium salts in psychiatric therapeutics./** Utilisation des sels de Lithium en therapeutique psychiatrique. Cahiers Medicaux (Villeurbanne). 1(10):753-756, 1975.

The use of lithium in clinical psychiatry is discussed, primarily in mood psychoses and schizoaffective states. Contraindications are renal insufficiency, low sodium regimens, hypothyroidism, and arteriosclerosis. A careful examination should be done before prescribing lithium. Lithium is available as lithium carbonate, and drinkable lithium gluconate ampulles. Lithium serum levels should range between 0.5and 1.0mEq. Signs of intoxication are tremor in writing, problems of equilibrium and coordination, hypertonia, and confusion. Side-effects are polyuria and polydipsia, digestive signs, and a psychological syndrome.

000612 Hallstrom, C. O. S.; Pare, C. M. B.; Rees, W. Linford; Trenchard, Ann; Turner, P. Departments of Psychological Medicine and Clinical Pharmacology, St. Bartholomew's Hospital, London, England **Platelet uptake of 5-hydroxytryptamine and dopamine in depression.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):40-44, 1976.

The uptake of 5-hydroxytryptamine (5-HT) and dopamine (DA) in platelet rich plasma (PRP) and the effect of protriptyline and clomipramine on this uptake was investigated in 39 outpatients with various types of affective disorder. Analysis of results showed no significant difference in uptake of either amine in PRP samples from subjects with neurotic depression, but a statistically significant reduction in mean 5-HT and DA uptake in patients with endogenous depression. Five patients who were given therapeutic doses of clomipramine showed a rapid reduction in 5-HT uptake, wheras no significant effect was demonstrated in eight patients receiving protriptyline. Findings suggest: 1) diminished 5-HT and DA uptake into platelets of depressed patients as compared to normal uptake neurotic patients; and 2) clomipramine exerts a significant blocking action in vivo on 5-HT uptake into platelets, and to a lesser extent on DA uptake. Comment on these observations in included, focusing on the mechanism of action involved in tricyclic drug effect on DA and 5-HT uptake, homovanillic acid levels in depressed patients, the possible antidepressant properties of L-dopa, and the behavioral effect of bromocriptine therapy on depressed patients. 9 references. (Author abstract modified)

000613 Hanck, Ch.; Collomb, H.; Boussat, M. Service de Psychiatrie, Centre Hospitalier de Fann, BP 5097, Dakar, Senegal **/Psychotic masked depression or black mask for depression./** Depressions masquees psychotiques ou masque noir de la depression. Acta Psychiatrica Belgica (Bruxelles). 76(1):26-45, 1976.

The possibility that the acute psychotic reaction frequent in Black Africa is in fact a manifestation of depression is examined in 10 case studies of acute psychosis from Zaire and Senegal. The depression criteria of Pichot and Hassan on masked depression was used and includes the following criteria: 1) evidence of depressive symptoms, 2) an underlying background and personality indicating depression; 3) evolutional characteristics; 4) familiar antecedents and hereditary factors; 4) responsiveness to antidepressive treatment. The ten cases analyzed were successfully treated with antidepressive drugs of the imipramine type without the use of neuroleptics. Sociocultural references aiding comprehension of the psychological framework of the African people such as perception of aggression and group orientation are presented. 12 references. (Author abstract modified)

000614 Heltberg, Jon; Larsen, Jens Knud; Kirk, Lars; Bjorum, Niels. Sct. Hans Hospital, afd D, DK-4000 Roskilde, Denmark **/Depression treated with FG-4963: results from an initial experiment./** Resultater af behandling of depressive tilstande med FG 4963 -- erfaringer tra hittidige pilotforsog. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):485-486, 1975.

The antidepressive effect of (+)trans-3((4-methoxyphenoxy)-methyl)-I-methyl-4-phenylpiperidine (FG-4963) is examined in 14 patients, diagnosed for endogenous depression. The dosages varied between 300 to 600mg per day. The study of the plasma concentration showed values from to 10-200 nanogram/ml. After treatment only 12 patients were included in the diagnosis. The effect of FG-4963 was certain in six cases, uncertain in one case and nonexistent in five cases. A correlation between the plasma level and the effect is not proved. The level was between 10-100 nanogram/ml in the six cases when an effect was obtained, and was seen after 3 weeks treatment. No serious secondary effects were observed. The results show an antidepressive effect. The effectiveness of FG-4963 is approximately the same as prevailing forms of treatment, but FG-4963 shows positive effects where tricyclic antidepressants have been ineffective.

000615 Horn, A. S. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Hills Road, Cambridge, England **The interaction of tricyclic antidepressants with the biogenic amine uptake systems in the central nervous**

system. Postgraduate Medical Journal (Oxford). 52(Suppl. 3):25-30, 1976.

The interaction of trycyclic antidepressants with the biogenic amine uptake systems in the central nervous system was examined to further assess evidence that functional abnormality of one or more of these amine systems is involved in the etiology of depressive disorders. Research findings indicate that tricyclic antidepressants inhibit uptake of noradrenaline (NA) and 5-hydroxytryptamine (5HT), and that this inhibition may be related to thier therapeutic effect in depression. This concept, however, is complicated before the effect becomes apparent. To clarify the relationship between the structure of these drugs and their action on uptake systems, studies of NA, 5-HT and dopamine (DA) uptake were performed on rat brain preparations using a number of different tricyclic compounds. It was found that their action on amine uptake depends on at least five structural and conformational features: 1) N-methylation of the terminal amino group; 2) changes in the length of the side chain; 3) alpha and beta methylation of the side chain; 4) substitution on the nucleus; and 5) changes within the nucleus. Comment on these observations is included, most of which focused on distinctions between uptake site and receptor site, the effect of amphetamine on DA and NA uptake, and differences in findings from in vitro and in vivo studies. 45 references. (Author abstract modified)

000616 Horrobin, David F.; Karmali, Rashida A.; Mtabaji, J. P.; Manku, M. S.; Nassar, B. A. Clinical Research Institute, 110 Pine Avenue West, Montreal, Canada **Prolactin and mental illness.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):79-85, 1976.

Experimental and clinical research which suggests that prolactin may be involved in some kinds of mental disorder, as may other pituitary hormones whose levels are influenced by changes in hypothalamic function, is reviewed. Abnormal prolactin levels which should be assessed individually rather than in terms of population norms, appear to be specifically involved in the premenstrual syndrome and in affective disorders responsive to lithium. Prolactin levels may provide a guide to the adequacy of anti-schizophrenic drug therapy. Further investigation into the role of prolactines in mental illness, particulary in mild depression, should be conducted in patients with mild, early disease in order to obtain more etiological information. Comment on these observations is included, focusing on the extreme variations which occur in daily plasma prolactin levels and the difficulty in interpreting hormone results, possible age correlations in prolactin levels, and differences between the mechanism of action in antipsychotic and other psychotropic drugs. 32 references. (Author abstract modified)

000617 Hullin, R. P. Department of Biochemistry, University of Leeds, Leeds, England **Metabolism of indole amines in depression.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):18-23, 1976.

Methods of studying indole amine metabolism and the role played by 5-hydroxytryptamine (5-HT) in the CNS functioning of depressed patients are discussed. Biochemical studies must use human subjects since no suitable animal analogues are available, but care must be taken in deducing changes in the 5-HT system from changes in tryptophan (TP) metabolites in the urine or CFS. Data obtained by direct study of the brains of depressives after suicide can also be deceptive. Pharmacologically, 5-HT function is best studied by loading tests with the precursor TP. There is evidence of disturbance of TP metabolism in depression, notably central depletion of 5-HT, but no proof that this plays a direct causal role. Comment on these observations is included, questioning the author's research with manic depressives in which serial fasting plasma total TP levels were determined in contrasting mood phases of five female bipolar patients. 41 references. (Author abstract modified)

000618 Jaskari, Martti O. Oulunsuuntie 140 as 6, 90220 Oulu 22, Finland **/Clinical aspects of Organon GB-94 vs amitriptyline./** Nagra kliniska aspekter pa Organon GB-94. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):473-474, 1975.

The antidepressive drug Organon GB-94 or mianserin is compared to amitriptyline in a double-blind experiment of 30 patients treated for 3 weeks and observed for 2 months. After 8 days the dosage was 80mg mianserin or 200mg amitriptyline per day. The antidepressive effect was observed after 7 to 9 days. Mianserin, contrary to amitriptyline, had a positive effect on the patient's paranoic symptoms. No secondary effects interrupted the therapy or resulted in reduction of the dosages. The most severe secondary effects were headaches and vertigo. Mianserin had no effect which would limit the patient's capability in normal work. The drug had no effect on somatic symptoms of depression. Due to the limited dosages, optimal results were not determined.

000619 Kariya, Tetsuhiko. Department of Neuro-psychiatry, Tokyo Medical and Dental University, Japan **Functional stimulation of drugs for the treatment of manic-depressive illness.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(2):197-204, 1975.

Research findings on the functional stimulation of monoamine oxidase (dopamine, norepinephrine), tricyclic antidepressants (imipramine, desipramine, tyrosine hydroxylase), and lithium on manic-depressives are presented, as well as research relating to animal studies. Examples of research cited are: function of tricyclic antidepressants such as imipramine in activating the synapsis by inhibiting the uptake of monoamine, the effects of L-5-hydroxytroptophan (L-5HTP) on manic-depressives by J. Fujiwara who found that there are depressives who react to either L-5HTP or L-DOPA; and N. Kato's finding that depressives who react to 5-HTP show a high concentration of homovanillic acid (HVA) before the treatment. 37 references.

000620 Kielholz, P. University Psychiatric Clinic, CH-4000 Basel, Switzerland **Long-term therapy of affective disorders and schizophrenia.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(3):93, 1976.

Introductory remarks to a symposium on long-term pharmacological treatment in psychiatry cite improvements in persons suffering from therapy resistant disorders by treatment with long-term antidepressive medication as well as prophylactic lithium therapy. Successful therapy must still begin with an exact diagnosis.

000621 Kim, Kwangiel. Department of Neuropsychiatry, School of Medicine, Hanyang University, Seoul, Korea **Antidepressants.** Neuropsychiatry (Seoul). 14(3):243-252, 1975.

Classification of depressed patients, biochemical etiology, and the pharmacokinetics and clinical application of antidepressants are discussed. The theory that the amounts of catecholamine and indolamine seem to be related to depression is reported. According to the characteristics of chemical structure there are three kinds of antidepressants: tricyclics, MAOI, and sympathomimetic stimulants. The chemical struc-

tures and reactions are presented in figures. There is no consensus as to the clinical effects of various antidepressants. Sixty one out of 93 studies published between 1958 and 1972 report that tricyclics are better than placebo. The use of antidepressants in relation to specific symptoms, side effects and possible problems is discussed. A dosage guide for antidepressants is included. 28 references.

000622 Kimura, M.; Nakagawa, T.; Ito, H. no address **A double-blind comparison of clinical efficacy of doxepin and imipramine in depressive patients.** Medicina Psicosomatica (Roma). 20(4):428-429, 1975.

A double-blind study comparing the efficacy of the antidepressants doxepin and imipramine in 191 depressive patients was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). The efficacy of the two drugs was compared after classifying patients by age, sex, and severity and types of depression. Results showed no significant difference between the two drugs as to general improvement. However, when efficacy on each somatic and psychological symptom was compared, significant difference was found between the two drugs. It is concluded that imipramine was more effective than imipramine in neurotic depression. This significant difference in efficacy for each symptom was recognized only within a period of 3 weeks of drug administration. No difference was found, however, in involutional depression. (Author abstract modified)

000623 Kragh-Sorensen, P.; Hvidberg, E. F.; Hansen, C. E.; Baastrup, P. C. Department O, State Mental Hospital, Glostrup, DK-2800, Denmark **Therapeutic control of plasma concentrations and long-term effect of nortriptyline in recurrent affective disorders.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(4):178-182, 1976.

A study was carried out to clarify some clinical pharmacological problems occurring during long-term treatment with nortriptyline. The possible prophylactic effect of the drug in recurrent affective disorders was examined in a group of patients with a high risk of recurrent episodes of unipolar manic-depressive disease. The value of monitoring plasma levels in order to achieve therapeutic control is demonstrated. Relapses during treatment over months and years were related only to insufficient plasma levels of the drug. The optimal therapeutic plasma range is 50ng/ml to 150ng/ml. 22 references. (Author abstract modified)

000624 Kurland, Morton L.; Hayman, Max. Desert Psychiatric Medical Group, 160 Luring Drive, Palm Springs, CA 92262 **A procaine derivative for the treatment of depression in an outpatient population.** Psychosomatics. 17(2):96-102, 1976.

A double-blind study comparing Gerovital H3 against placebo in an outpatient population with diagnoses of depressive disorders was performed. Private practice patients (n=63) were rated before and after treatment by the Clinical Global Impression, Hamilton Rating Scale and the Zung Self-Rating Scale. Statistical analyses using the T-test were performed. It is concluded that Gerovital H3 is an efficacious drug in the treatment of mild to moderate depression, and exhibits minimal side effects or complications. Long-term and short-term comparison tests with geriatric mental patients, using procaine hydrochloride and placebos, showed no significant differences in the amelioration of depressive symptoms. 18 references.

000625 Lee, Sang Yeon; Kwak, Dong Il; Lee, Byung Yoon. Department of Neuropsychiatry, College of Medicine, Korea University, Korea **Lithium maintenance therapy.** Neuropsychiatry (Seoul). 14(3):302-305, 1975.

Twelve case studies of manic-depressive psychoses under lithium maintenance treatment were presented. Results are as follows: 1) only four patients out of 11 who had no recent recurrences showed .6-1.2mEq/L in their serum lithium level; 2) one patient, who was controlled for about 12 months with 600mg of lithium carbonate, had another attack 10 months after quitting the maintenance treatment; and 3) there was no evidence of interrelationships among body weight, serum lithium level and maintenance dosage. Studies on the lithium maintenance treatment were briefly reviewed. 17 references. (Author abstract modified)

000626 Legg, Joseph F.; Stiff, Margaret P. Department of Psychiatry, Hartford Hospital, Hartford, CT 06115 **Drug-related test patterns of depressed patients.** Psychopharmacology (Berlin). 50(2):205-210, 1976.

The effects of imipramine, chlorpromazine and placebo on a wide range of psychological tests were assessed in a double-blind study in 49 hospitalized depressed patients. Neither imipramine nor chlorpromazine produced impairment on most measures of intellectual functioning. The results suggest that imipramine may impair ability to assimilate and retain information, and that chlorpromazine may impair sustained attention. The differential effects are discussed in relation to symptoms and to hypotheses about the relationship between arousal and chlorpromazine and between retardation and imipramine in the treatment of depression. 29 references. (Author abstract modified)

000627 Lopez-Ibor Alino, J. J.; Ayuso Gutierrez, J. L.; Montejo Iglesias, M. L. Av. Nueva Zelanda 78, Madrid 35, Spain **5-Hydroxytryptophan (5-HTP) and a MAOI (nialimide) in the treatment of depressions: a double-blind controlled study.** International Pharmacopsychiatry (Basel). 11(1):8-15, 1976.

Through a controlled double-blind study in 30 hospitalized patients affected with endogenous depression, the antidepressant action of the combination of nialamide plus levo-5-hydroxytryptophan (l-5-HTP) has been evaluated and compared with a control group which only received nialamide plus placebo. The patients treated with nialamide plus l-5-HTP achieved a fuller recovery than those who were treated with nialamide alone. The treatment with nialamide plus l-5-HTP proved to have a shorter delay of onset. Side-effects showed no marked differences except for the orthostatic hypotension which was less apparent in those patients treated with nialamide plus l-5-HTP. 8 references. (Author abstract)

000628 Luchins, D.; Ananth, J. Department of Psychiatry, St. Mary's Hospital, 3830 Lacombe Avenue, Montreal, Quebec, H3T 1M5, Canada **Therapeutic implications of tricyclic antidepressant plasma levels.** Journal of Nervous and Mental Disease. 162(6):430-436, 1976.

Relevant research on therapeutic implications of tricyclic antidepressant plasma levels is reviewed, emphasizing that methodological advances in drug assay techniques have made their measurement more frequent. Plasma levels of tricyclics have been correlated with diagnosis, prognosis, clinical response and side-effects. But even in the area most extensively examined, the correlation between plasma level and clinical response, the results have been conflicting. Different studies have suggested that there is no relationship between

plasma level and clinical response, as well as positive and negative correlations, and even a curvilinear relationship. Therefore, impossible to define a therapeutic range that will be applicable to depressed patients as a group. For the moment, the problem of finding a suitable therapeutic dose for the individual patient remains of paramount importance. Studies to date suggest the need to consider genetic factors, previous and present use of other drugs, the possibility that therapeutic failure might be a result of too high as well as too low a dose, as well as the possible relationship between high plasma levels and side-effects. Since for the specific individual, the metabolism of different tricyclic antidepressants is similar, it may be useful to adjust dosages until a therapeutic one is obtained, instead of immediately switching to another medication. Although the usefulness of routine plasma level determination remains to be established, this technique may be indicated in cases of intractable depression and remains an important research tool. 31 referenc es. (Author abstract)

000629 Lund, J.; Bechgaard, E.; Heltberg, J. P.; Larsen, J. K. A/S Ferrosan, Sydmarken 5, DK-2860 Soborg, Denmark **/Pharmacokinetic studies of FG-4963./** Farmakokinetiske undersogelser af FG 4963 pa patienter. Norkisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):483-484, 1975.

The pharmacological effects of the antidepressant (+)trans-3((4-methoxyphenoxy)-methyl)-I-methyl-4-phenylpiperidine (FG-4963) is examined on seven patients. The course of the plasma concentration was studied for 50 hrs after one oral dose of 500mg. The course of the concentration is described as a two compartment open model. The parameters were evaluated by computer analysis. The results show a great daily variation of the plasma concentration compared to tricyclic antidepressants. 4 references.

000630 Maas, James W. Department of Psychiatry, Yale University School of Medicine, New Haven, CT **Catecholamines and depression: a further specification of the catecholamine hypothesis of the affective disorders.** In: Friedhoff, A., Catecholamines and behavior. Vol. 2. New York, Plenum Press, 1975. 225 p. (p. 119-133).

Recent research findings are detailed which support the view that depression is a biochemically heterogeneous illness, and that two subtypes of depression can be biochemically and pharmacologically identified. Excretion levels of the norepinephrine metabolite, 3-methoxy-4-hydroxyphenethylaneglycol (MHPG) can be used as an identifiable trait for distinguishing certain types of depression and as a tool in determining for that type what drugs are most effective. The effects of imipramine, demethylimipramine, d-amphetamine and amitriptyline on the biochemical mechanisms in affective disorders are discussed. 78 references.

000631 Majczak, Adam; Masiak, Marek; Grzywa, Anna; Gorniewicz, Anna; Komada, Joanna. Klinika Psychiatryczna AM, ul. Abramowicka 2, 20-442 Lublin, Poland **/Application of Sinequan in the treatment of various clinical forms of depression./** Zastosowanie Sinequanu w leczeniu roznych form klinicznych depresji. Psychiatria Polska (Warszawa). 9(1):51-57, 1975.

Sinequan (doxepin) was administered in doses of 75-450mg/day to 34 depressive patients (23 females and 11 males, average age 45.9years) for 1 month. Of this group, 12 were outpatients. Significant improvements were observed in all cases. The drug acts primarily on the depressed mood of the individual, and, to a lesser extent, on thought disturbances of the depressive type, e.g. feelings of guilt and paranoia. Side-effects were rare and mild. 12 references.

000632 Mandell, Arnold J.; Knapp, Suzanne. Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093 **A neurobiological model for the symmetrical prophylactic action of lithium in bipolar affective disorder.** Pharmakopsychiatrie Neuro-psychopharmakologie (Stuttgart). 9(3):116-125, 1976.

By treating rats with lithium chloride or cocaine hydrochloride, or lithium chloride followed by cocaine hydrochloride, the antagonistic effects of these drugs on two mechanisms that may be involved in regulating serotonin (5-HT) synthesis in the striate cortex has been demonstrated. Lithium chloride stimulates the relative velocity of the active uptake of labelled tryptophan and proportionally enhances the conversion of labelled trytophan to 5-HT in synaptosomally enriched preparations. With continued administration of lithium chloride, the activity of tryptophan hydroxylase from the median raphe and subsequently in lysed synaptosomal preparations from striate cortex is reduced; the substrate uptake remains enhanced, but the conversion of substrate to transmitter returns to control levels. In contrast, an injection of cocaine hydrochloride inhibits the high affinity uptake of tryptophan, reducing the conversion of the amino acid to 5-HT and resulting in an increase in the biosynthetic enzyme activity. However, administration of cocaine hydrochloride after three daily lithium chloride injections results in no apparent effects on substrate uptake, conversion, or enzyme activity. It is theorized that the effect of lithium was to push two regulatory parameters (the uptake of substrate and the enzyme activity) to their respective functional upper and lower limits, leaving the serotonergic neurons "buffered" against the "usual" effects of the stimulant drug. This neurobiological model is offered for consideration in relation to the clinical effects of lithium in the prophylaxis of both mania and depression in some patients. 40 references. (Author abstract)

000633 Mazzella, G. L.; Lombardi, M.; Bo, P.; Massarini, M. Clinica delle Malattie Nervose e Mentali, University of Pavia, Pavia, Italy **/Clinical study of a new form of dibenzepine, with protracted action./** Studio clinico di una nuova forma farmaceutica, ad azione retard, della dibenzepina. Rassegna di Studi Psichiatrici (Siena). 65(4):723-734, 1976.

A long acting form of dibenzepine (240mg tablets) was tested for effectiveness in 30 patients, male and female, 22 to 82 years old, with forms of depression. Results showed that this retard action drug is both safe and therapeutically effective. 39 references.

000634 Meltzer, Herbert L.; Rosoff, Carl J.; Kassir, Suham; Fieve, Ronald R. Dept. of Internal Medicine, New York State Psychiatric Institute, New York, NY 10032 **Active efflux of lithium from erythrocytes of manic-depressive subjects.** Life Sciences (Oxford). 19(3):371-379, 1976.

Erythrocytes were obtained from manic-depressive patients who had been treated with lithium for therapeutic and prophylactic purposes, and efflux rates were measured at 37 degrees centigrade under conditions designed to approximate the in vivo state as closely as possible. The lithium transport kinetics are characterized by asymmetric rate constants of efflux and influx. The efflux constants, which are more than twice as large as the influx constants, correlate well with the in vivo distribution of lithium between erythrocytes and plasma. The efflux process, which is not inhibited by ouabain and is, therefore, distinct from the sodium potassium pump, is characterized by Michaelis-Menten kinetics and a large energy of activation. There appears to be a normal endogenous inhibitor which regulates the activity of the postulated lithium pump. 10 references. (Author abstract modified)

000635 Miller De Paiva, L. no address **Psychosomatic study of neurotic and psychotic depression. Results of the group therapy.** Medicina Psicosomatica (Roma). 20(4):352, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975), paper describes a study of 47 patients for whom complete biochemical profiles (PBI, cholesterol, lipoproteins, dosage, and the Exton-Rose test in the blood and 17/Ks, 17/OHCS, VMA, aldosterona, and dehydroepiandrosterone dosages in the urine) were available indicating the following: 1) neurotic depression does not present a characteristic biochemical profile; 2) psychotic depression may be distinguished from neurotic depression by a higher rate of dehydroepiandrosterone excretion in psychotic depression; 3) in different types of psychotic depression (involutive, manic-depressive, and depression in schizophrenia) there is special biochemical profiles; and 4) the increase in urinary excretion of dehydroepiandrosterone and of the beta/alpha lipoprotein ratio proved an index to the gravity of depressive states and the propensity towards suicide. After diagnosis, 36 patients were given two types of treatment: 13 cases received only antidepressant (imipramine or phenelzine) and anxiolytic (benzodiazapinone) drugs, and 23 patients received these drugs plus psychoanalytic group therapy. The following conclusions are drawn: 1) antidepressant drugs fail to act in reactive depression; 2) patients who were able to stop medication presented diagnosis of depressive neurosis with normal excretion of dehydroepiandrosterone; and 3) the increase of dehydroepiandrosterone was evidence of the probable existence of a propensity towards lifting of depression following drug suppression. (Author abstract modified)

000636 Miura, Wataru; Yamada, Hiroshi. Kuriyama Red Cross Hospital, Japan **The effect of clomipramine (anafranil) on continuing pain.** Psychiatria et Neurologia Japonica (Tokyo). 77(10):747, 1975.

The effects of the tranquilizers imipramine and carbamazepine in reducing continuing pain in patients is well known, so clomipramine, a derivative of imipramine, was tested to see if it had a like effect. Following an IV injection of 25-50 mg of clomipramine an antipain effect was noted. Subjects had experienced spontaneous pain on one side or numbness due to thalamus damage, but did not show paralysis of the motor nerves. They had walking or sitting difficulties. It was thought that both the tranquilizing effect of the drug and its activity on the central nervous system were important factors in pain reduction.

000637 Moller, Svend E.; Kirk, Lars; Fremming, Kurt H. Forskningslaboratorium D, Sct. Hans Hospital, DK-4000 Roskilde, Denmark **/The effect of plasma aminoacids on depression./** Plasma aminosyre monstret hos manio-depressive patienter. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):461-462, 1975.

The insufficient supply of tryptophan (TRY) in depressed patients is studied. A total of 24 persons were in the trial, 12 depressed patients and a control group. Blood tests were analyzed as to aminoacids (valin, isoleucin, leucin) and TRY. Eight grams TRY were given daily every morning. The ratio (R=TRY/val + ISO + LEU) decreased with age. Three patients remitted after 1 week's treatment with TRY. Their R-values were extremely low compared to the same age in the control group. The positive response to TRY therapy is explained by the insufficient supply of TRY in the plasma. The deficit among the nonrespondents is due to the reduced activity of the drug transport mechanism. 5 references.

000638 Moody, J. P. Department of Biochemistry, Royal Dundee Liff Hospital, Dundee, Scotland **Some aspects of the metabolism of tricyclic antidepressants.** Postgraduate Medical Journal (Oxford). 52(Suppl 3):59-61, 1976.

The pharmacokinetic properties of tricyclic antidepressants are briefly described, including physicochemical characteristics, metabolic fate, and disposition in the body. Recent progress in measuring their half-life and volume of distribution is also treated. Evidence suggests that the bioavailability of the drugs differs from subject to subject, from compound to compound and even within individuals. Although factors that may be responsible for intrasubject variability have just begun to be studied, results should be considerably valuable to the clinical pharmacologist as well as the clinician. Comment on these observations is included, focusing on the degree to which the drugs bind to plasma proteins and length of time required for the free antidepressant to reach a steady state in the plasma. 19 references. (Author abstract modified)

000639 Morin, J.-Y.; Deferdinando, A.; Rannou, J.-M. no address **/Clinical trial of 5-HTP./** Essai clinique du 5 H.T.P. Revue de Neuropsychiatrie de L'Ouest (Rennes). 12(49):3-26, 1975.

A study done on 10 alcholic and 50 aged patients suffering from symptoms of depression and their reaction of doses of 5-hydroxytryptophan (5-HTP) in conjunction with regularly prescribed transquilizers, neuroleptics and anxiolytics is described. Because serotonin plays a large role in depression, 5-HTP was given combined with vitamin B6 which, by carboxylation, was synthesized into serotinin. Tolerance to the treatment was excellent; only six out of sixty had ill effects. Results show the disappearance of melancholias, guilt feelings, hypochondria, the reduction of the slowing down of psychic processes and motor functions, indicating that 5-HTP is a pure antidepressant useful in the treatment of the elderly.

000640 Mountjoy, C. Q. Department of Psychological Medicine, University of Newcastle upon Tyne, Newcastle upon Tyne, England **The possible role of thyroid and thyrotrophic hormones in depressive illness.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):103-107, 1976.

Research on the possible role of thyroid and thyrotrophic hormones in depressive illness is reviewed, focusing on new findings which appear to question two 1972 reports which showed that injection of thyrotrophin releasing hormone (TRH) had a mild antidepressant action of rapid onset and produced a low thyrotrophin (TSH) response in some depressed patients. Because TRH appeared to act rapidly on depression, it was thought to be of possible value as an initial adjunct to tricyclic antidepressant or ECT, but the weight of evidence from subsequent controlled trials does not support the original observation. Trials with triiodothyronine have, however, demonstrated marginal enhancement of the antidepressant action of imipramine, particularly in some women, although this appears of more theoretical than therapeutic interest. The original evidence of a reduced TSH response to TRH in some depressed patients has been confirmed, but not yet exploited to differentiate subtypes of depression or to predict the results of antidepressant therapy. Comment on these observations is included, focusing on the effects of thyroid hormones on tissue amines and the difficulties of generalizing findings from animal studies to develop a model of depressive illness in humans, and hypersensitivity to clomipramine side-effects in some patients in hot climates. 31 references. (Author abstract modified)

000641 Moyes, I. C. A.; Moyes, R. B. Department of Psychiatry, Broadgate Hospital, Walkington, Beverley, North Humberside, England **Further developments in the study of 3',5'-cyclic adenosine monophosphate in relation to psychiatric illness.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):110-114, 1976.

Developments in the study of 3',5'cyclic adenosine monophosphate (cAMP) in relation to psychiatric illness are reviewed, emphasizing that various factors, including circadia and menstrual changes, have been shown to influence levels of urinary cAMP excretion. Others, such as diet, exercise and age, have been postulated, but not confirmed. The effect of psychotropic drugs on cAMP excretion remains uncertain, despite suggestive experimental evidence. In manic-depressive states, cAMP excretion rates have generally not correlated with mood. Depressed patients, however, do appear to have low urinary excretion of cAMP, with recovery to normal levels as mood improves on antidepressant therapy and/or ECT. In contrast to earlier work, a preliminary experiment reported herein showed no significant effect of ECT as such on cAMP. It is concluded that the possibility that anxiety might alter levels of cAMP excretion is worthy of study, as agitation is a prominent feature of some forms of depressive illness and it is is a common concomitant of neurotic depression. Comment of these observations is included, focusing on measurement of cyclic AMP measurements in plasma and other body fluids. 31 references. (Author abstract modified)

000642 Murguia, Daniel. no address **/Conference on depression in Rio de la Plata./** Coloquio rioplatense sobre depresion. Acta Psiquiatrica y Psicologica de America Latina (Buenos Aires). 21(3-4):168-169, 1975.

A brief summary of a conference (1975) on depression held in Buenos Aires under the auspices of the Argentinian Association of Biological Psychiatry, the Argentinian Society of Neurological, Psychiatric, and Neurosurgical Sciences, and the Edmundo Fischer Psychiatric Center is presented. Topics discussed include: the evolution of biochemical knowledge of depression; biogenic amines and the catecholamine theory of depression; the contribution of Fischer toward a new concept of depression; the relationship between analysis of the depressed state and the depressed person; depression masked by somatic symptoms; tardive depression; the classification, indications and secondary effects of various antidepressants, including Trazodone.

000643 Nick, J.; Luaute, J. P.; Des Lauriers, A.; Moinet, A.; Monfort, J. Clinque Neurologique de l'Hopital Tenon, 4, rue de la Chine, F-75020 Paris, France **/A controlled study of the association of clomipramine and lithium./** L'association clomipramine-lithium essai controle. Encephale (Paris). 2(1):5-15, 1976.

The efficacy of clomipramine plus lithium carbonate was compared to that of clomipramine plus placebo in a controlled study performed on 30 patients of both sexes, all having recurrent depressions. The control was a double-blind study with random sampling of patients. Results were recorded by an independent observer using a rating scale and were analyzed statistically. In spite of the bias observed it seems possible to conclude that the association of clomipramine plus lithium carbonate has no greater global antidepressive efficacy as compared with clomipramine plus placebo which means that lithium does not potentialize nor antagonize the antidepressant effect of clomipramine. Due to the limited number of patients -- bipolar depression (10 cases) unipolar depression (20 cases) -- it was not possible to study the results in these 2 subgroups. 27 references. (Author abstract modified)

000644 Ohara, Kenjiro; Komatsu, Junichi; Matsui, Takeo. Department of Psychiatry and Neurology, Jikei University School of Medicine, Japan **Clinical experience of Sepazon (Cloxazolam) for depressive manic.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(6):711-718, 1975.

A minor tranquilizer, Sepazon, which has been used mainly for neuroses, was given to patients with depression with favorable results. Sepazon (cloxazolam), is pharmacologically similar to diazepam, and yet has a better tranquilizing effect and a lower toxicity than diazepam. It contains an anticonvulsant and a muscular relaxant. Sepazon was given to 13 male and 19 female outpatients. All cases had depression as the main symptom with 15 cases of endogenous depression, 9 neuroses, 4 schizophrenia, 1 epilepsy, 1 reactive depression, 1 depression with arteriosclerosis of the brain and 1 psychosis. All cases were examined at least once a week and evaluated according to the prepared three level criteria. General evaluation was made on the fourth week. The results were: 14 (43.8%) significantly effective, 9 (28.1%) effective, 5 (15.6%) fairly effective, and 3 (9.4%) ineffective. Sepazon was also effective for anxiety, imsomnia and tension. Though Sepazon is characterized as a minor tranquilizer, favorable clinical results suggest a future wide use of this drug as an antidepressant. 8 references.

000645 Paes de Sousa, M.; Souto Lopes, J.; Figueira, Luisa; Neves Cardoso, J. Servico de Psiquiatria, Hospital de Santa Maria, Av. Egas Moniz, Lisbon, Portugal **/Comparative study of three psychotropic drugs in the treatment of depressions./** Etude comparative de trois psychotropes dans le traitement des depressions. International Pharmacopsychiatry (Basel). 11(1):43-64, 1976.

The effect of three antidepressive psychotropes (chlorimipramine, doxepin and dibenzepin) was studied in 107 depressed patients. In each patient the mean value of twelve symptoms was evaluated and compared weekly (for 4 weeks), by statistical methods. In addition, the effect of each drug was analyzed in personality variables. A thymeretic and thymoanaleptic rapid action on corporality and 'endothymic-vital' layer was found with chlorimipramine. Doxepin acts rapidly with sedative and anxiolytic actions on reactive symptoms related with personality superstructures having long term antidepressive effects. Dibenzepin has a thymeretic rapid and intensive action and a slow thymoanaleptic effect on the same personality stratus of chlorimipramine. 52 references. (Author abstract)

000646 Paykel, E. S.; DiMascio, A.; Klerman, G. L.; Prusoff, B. A.; Weissman, M. M. St. George's Hospital and Medical School, London S.W.17, England **Maintenance therapy of depression.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(3):127-136, 1976.

Findings from a study of maintenance treatment in predominantly neurotic depressives responding to initial treatment with amitriptyline are summarized. Patients were continued on amitriptyline for 8 months, withdrawn double-blind to placebo after 2 months, or withdrawn overtly to no medication, with and without individual psychotherapy from social workers in a factorial design. Continuation significantly reduced early relapse and symptom return, compared with either condition of early withdrawal. Psychotherapy improved social adjustment after 8 months in patients who did not relapse, without any significant interactions. Side-effects were minimal, except for carbohydrate craving. These findings suggest that tricyclic antidepressants should be routinely continued for several months after drug induced remission. 27 references. (Author abstract)

000647 Prange, Arthur J., Jr. University of North Carolina, Chapel Hill, NC 27541 **Acceleration of antidepressants by thyroid hormone.** Psychopharmacology Bulletin. 12(3):84, 1976.

The relationship between endocrine hormones and clinical disorders such as hyperkinesis, depression and schizophrenia is studied in humans and in animals. The effect of thyrotropin releasing hormone (TRH) injections in schizophrenic patients and in women with unipolar depression is partial and unpredictable. In tests with normal woman subjects, TRH was administered 24 hours after small oral doses of thyroxine and L-triiodothyromine (to block pituitary response); it was found that the more TRH release is diminished, the greater the euphoric response to administered TRH. Preliminary animal studies indicate that pituitary blockade results in greater uptake by the brain of administered TRH. The effects of TRH injection preceded by oral thyroid hormone administration in treating depression in humans is now being studied. Studies in mice reveal that TRH antagonizes the sedation caused by barbiturates but enhances the anticonvulsant activity of phenobarbital against electrically induced seizures. An analog of TRH is even more effective in this regard. Other animal studies show that certain analogs of TRH are more potent barbiturate antagonists than TRH itself but less potent as thyrotropin (thyroid stimulating hormone, TSH) releasers than TRH. The lack of identity between central responses and pituitary responses suggests the existence of a central receptor mechanism.

000648 Prusoff, Brigitte; Weissman, Myrna M. Yale University School of Medicine, New Haven, CT **Followup of maintenance treatment for depression.** Psychopharmacology Bulletin. 12(3):84-85, 1976.

The long-term implications of psychotherapy and amitriptyline therapy in the treatment of depression were examined. Patients received amitryptiline, alone or with psychotherapy, for 8 weeks. At the end of 8 weeks, patients were subdivided into three groups: amitriptyline, placebo, or no medication. Followups were conducted 6 months and 12 months later. Maintenance pharmacotherapy, with or without psychotherapy, is most effective in preventing relapse. Psychotherapy does not affect relapse rates but it produces a gradual improvement in social functioning in patients who remain asymptomatic. After 1 year, 10% of the patients remained chronically symptomatic, 60% had mild recurring symptoms and 30% were asymptomatic. When the subgroups who remained symptomatic were examined, it was found that 67% had been assigned to the no medication group.

000649 Rafaelsen, Ole J.; Mellerup, Erling T.; Shapiro, Robert W. Psychochemistry Institute, Rigshospitalet, 9 Blegdamsvej, DK-2100 Copenhagen, Denmark **Lithium in the living organism: is an integrated hypothesis feasible?** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(3):108-115, 1976.

Following a review of acute and long-term lithium effects on electrolyte metabolism which are demonstrable and reproducible in man, an integral hypothesis to explain lithium action in human manic-depressive disorders is tested for feasibility. The results are consistent with one of the following two hypotheses: a) that lithium acts by membrane stabilization, and/or b) that lithium acts by interplay with magnesium on one or more enzymes. The above findings and hypotheses direct attention to membrane dysfuction as the basic defect in manic/melancholic states. This may find support in preliminary findings of special HL-A antigen profiles in unipolar and bipolar manic/melancholic patients. A four type pump defect model to account for the various clinical types of affective disorders is proposed. 32 references. (Author abstract modified)

000650 Renard, P.; Bourel, J.; Samjee, A.; Joubrel, M; Remy, F. no address /**Concerning propizepine hydrochlorate and its indications in depression.**/ A propos du chlorhydrate de propizepine et de ses indications dans les depressions. Revue de Neuropsychiatrie de L'Ouest (Rennes). 12(49):45-51, 1975.

The use of propizepine hydrochlorate is described in the treatment of alcoholics with depressive symptomatology. Twenty four patients, hospitalized for alcohol intoxication, all suffering from various types of depression, were given doses varying from 100mg/day to 200mg/day. It was found that the treatment had a 60% rate of improvement in those suffering from neurotic depression or reactive depression with lesser improvement for patients with manic-depressive diagnoses or involutional depression. The antidepressant shows better tolerance and manageability than other tricylic derivatives.

000651 Renfordt, E.; Busch, H. Psychiatrische Klinik der Freien Universitat Berlin, Nussbaumallee 36, D-1000 Berlin 19, Germany /**New strategies of psychiatric diagnosis using audiovisual techniques: 1. use of time blind video analysis for evaluation of antidepressant drug trials.**/ Neue Strategien psychiatrischer Urteilsbildung durch Anwendung audiovisueller Techniken. 1. Mitteilung: Verlaufsuntersuchung einer antidepressiven Therapie durch vergleichende und zeitblinde Auswertung von Fernsehaufnahmen. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(2):67-75, 1976.

Audiovisual recordings of patient interviews were used in a double-blind comparison of amitriptyline and the tricyclic drug mianserin (Tolvin) in 20 depressed patients, including 10 males and 10 females, average age 48 years. Eleven patients received an average dose of 150mg/day amitriptyline, and nine patients received 60mg/day mianserin. Two raters made diagnostic decisions based on random presentation of audiovisual recordings of 35 to 45 minute interviews with the patients on the day before treatment, and the 10th and 20th days of treatment. Depression was rated by global impression. Both raters gave the same results. Patients receiving amitriptyline improved steadily, while patients receiving mianserin showed improvement between day 0 and day 10, but become worse between day 10 and day 20. This method is represented as providing significant progress in the assessment of a drug's profile in time. 21 references.

000652 Ridges, A. Pauline. Clinical Laboratories, Fazakerley Hospital, Liverpool, England **The potential value of biochemical parameters in the diagnosis and medication of affective disorders.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):9-16, 1976.

Studies of biogenic amine metabolites in the urine of depressed patients are reviewed to demonstrate the potential value of biochemical parameters in diagnosing and treating affective disorders. The different types of depression cannot be clearly differentiated on clinical criteria, and although the response to specific antidepressant therapy may clarify the diagnosis, it can only do so retrospectively. Measurements of the cerebral amine metabolites in body fluids show promise in providing an earlier means for identifying subgroups of depressed patients and for predicting therapy response. Studies of specific catecholamine and indoleamine metabolites have shown correlations with certain types of depression, and the activity of the serotinergic system appears to be reduced in some depressed patients. Further work may enable biochemical characterization of the various subgroups and thus tailor

therapy to individual patients' needs. Comment on these observations is included, most of which focuses on discrepancies between the findings of various researchers and difficulties in determining causes for the different patient responses to antidepresant drug therapy. 92 references. (Author abstract modified)

000653 Saito, Masami. Department of Psychiatry and Neurology, Kansai Medical University, Japan **Clinical-physiological study of drugs for the treatment of psychoses.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(2):175-187, 1975.

Techniques and results of recent clinical studies of psychotropic drugs used in the treatment of psychoses are presented. Included are: 1) quantitiative analyses of EEG and the results of a computer classification of EEG and sleep; 2) analyses of EEG and REM patterns obtained from antianxiety drugs, antidepressant, major and minor tranquilizers, neuroleptics, and psychotropic drugs; and 3) the relationship between psychopathology and evoked responses from tricyclic antidepressants, lithium, and antianxiety drugs. 54 references.

000654 Satomi, Ryuta; Asano, Yu; Okada, Fumihiko; Saito, Yoshiro; Fujieda, Toshiyoshi; Daiguji, Shin; Yamashita, Kaku; Suwa, Nozomu. Department of Neuropsychiatry, Hokkaido University, Japan **Psychopharmacological drug densities in the blood serum -- densities of tricyclic antidepressants and their meaning.** Psychiatria et Neurologia Japonica (Tokyo). 77(10):746, 1975.

Blood serum levels of tricyclic antidepressant drugs such as amitriptyline (AT), nortriptyline (NT), imipramine (IP), and desipramine (DP) were measured in depressed patients. NT was detected in the blood serum of patients taking AT. Demethylation and hydroxylation due to enzyme action was noted in differing degrees in patients taking these antidepressants. Differences are said to be due to the ratio of hydroxylation.

000655 Scoggins, Bruce A.; Coghlan, John P.; Maguire, Kay; Burrows, Graham D.; Davies, Brian. Howard Florey Institute of Experimental Physiology and Medicine **The measurement of plasma levels of tricyclic antidepressant drugs.** Australian and New Zealand Journal of Psychiatry (Carlton). 10(1):7-12, 1976.

A double isotope derivative dilution procedure for measuring plasma levels of nortriptyline is described. The assay is specific, sensitive, precise, and reproducible. Studies on the variation in steady state plasma levels are described on a fixed oral dosage of nortriptyline. Between individual variations in steady state plasma levels are large. Between day within individual variation is 15-20%. Dosage regime, time of blood sampling after last oral dose, and the method of blood handling are unlikely to affect the steady state plasma levels. Within an individual, the oral dose, duration of treatment, and concomitant drug treatment are all important determinants of the steady state plasma level. 29 references. (Author abstract)

000656 Scotto, J.-C; Dufour, H.; Huber, J.-P.; Crespin, J.; Pin, M.; Joseph, A.; Sutter, J. M. Clinique Psychiatrique, Universitaire de la Faculte de Medecine de Marseille, Hopital de la Timone, F-13385 Marseille, France **/Amitriptyline in psychiatric therapy: eight years of usage in hospital practice./** L'amitriptyline en therapeutique psychiatrique: a propos de huit annees d'utilisation en pratique hospitaliere. Encephale (Paris). 2(1):61-72, 1976.

One hundred cases of depression treated with amitriptyline were examined to determine the therapeutic value of this antidepressant. The sample consisted of subjects suffering from melancholia, neurotic and/or reactional depression and depressive states associated with psychoses (schizophrenic or nonschizophrenic) who were hospitalized in a psychiatric clinic in Marseille. Results confirm that amitriptyline remains one of the most effective, manageable and well tolerated antidepressants, especially in the treatment of depressive states related to a high level of anxiety in patients under 60 years of age.

000657 Shaw, D. M. MRC, Department of Psychological Medicine, Whitchurch Hospital, Cardiff, Wales **Tricyclic antidepressants, tryptophan and affective disorder.** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):47-50, 1976.

Possible explanations for the mechanism and the delayed onset of action of tricyclic antidepressants in affective disorders were investigated. A controlled trial with three experimental groups determined the relative roles on the aminergic systems in depression and its therapy. Results can be interpreted in various ways, one possibility being that recovery from depression may involve additional factors connected with the nature of the illness itself and/or with the therapeutic activity of the drug used to treat it. This theory was further examined by studying tryptophan's role in affective illness and of the changes observed after treatment. Findings suggest the involvement of an additional factor, as yet unidentified. It is speculated that the abnormality in depression lies somewhere in the 'amine area' and also may involve changes in peripheral tryptophan distribution and metabolism, with other factors acting as additional secondary movers. Comment on these observations is included, focusing on unknown quantities which affect success or failure in tricyclic antidepressant therapy, research using tryptophan and monoamine oxidase inhibitors to test the single amine hypothesis, the role of receptor sensitivity in treatment outcome, and the effect of combined treatment with L-dopa and tryptophan. 6 references. (Author abstract modified)

000658 Sinclair, J. M.; Walsh, M. R. no address **Treatment of anxiety and depression states in aged patients. Double-blind comparison of the effects of amitriptyline and a fluphenazine-nortriptyline combination.** Age and Ageing (London). 4(4):226-231, 1975.

Amitriptyline was compared with a fluphenazine/nortriptyline combination in a double-blind 4 week trial in 72 aged patients of 65 years or older who had anxiety and depression. Efficacy was evaluated by a clinical scale completed by the physician and another scale completed by the patient. The fluphenazine/nortriptyline combination appeared to have superior therapeutic action, and side-effects were rarer than with amitriptyline alone. 11 references.

000659 Szemis, Andrzej. Instytut Psychoneurologiczny, Al. Sobicskiego 1/9 02-957, Warsaw, Poland **/Skin reactivity to histamine in schizophrenics and other psychiatric patients./** Reaktywnosc skorna na histamine chorych na schizofrenie i chorych z innymi zaburzeniami psychicznymi. Psychiatria Polska (Warszawa). 10(2):121-127, 1976.

To test the view that schizophrenics exhibit lowered skin reactivity to histamine, a histamine skin test was performed on 102 psychiatric patients prior to pharmacological therapy or during a drug free period. The following diagnostic categories were included in the study: schizophrenia of recent origin; chronic schizophrenia; other psychoses; depression; nonpsychotic disorders. A group of 42 healthy persons served as a control. Results showed that the reactivity of untreated patients with recent history of illness (including schizophrenia)

is significantly higher than that of the control group, while reactivity of patients during pharmacological treatment was significantly lower. This indicates that psychotropic drugs significantly lower skin sensitivity to histamine, although some patients showed no decrease in histamine reactivity even while receiving high doses of psychotropic drugs. Skin reactivity to histamine of chronic schizophrenics during the drug free period did not differ significantly from that of healthy persons and short-term schizophrenics. 25 references. (Author abstract modified)

000660 Szlabowicz, Jerzy Wieslaw. Klinika Chorob Psychicznych, AM, ul. Debinki 7, 80-211 Gdansk, Poland /**Clinical studies on the antidepressant action of lopramine.**/ Badania kliniczne nad przeciwdepresyjnym działaniem lopraminy. Psychiatria Polska (Warszawa). 10(2):139-145, 1976.

In a trial of a new antidepressant, lopramine (dibenzazepine) was administered to 12 women and 10 men with endogenous cyclic depression. The average of the patients was 50 years. Dosage was between 140mg and 280mg daily for three weeks. Full recovery occurred in 16 cases, partial recovery in two, slight improvement in two, and there was no change in two cases. Results began to be observable during the first week of treatment. Lopramine is particularly effective in counteracting depressive moods and lowered drive. Although similar in action to the antidepressant imipramine, none of the side-effects of imipramine were observed. 12 references. (Author abstract modified)

000661 Todrick, A.; Tait, A. C. Crichton Royal Hospital, Dumfries, Scotland **What are tricyclic antidepressant drugs?** Postgraduate Medical Journal (Oxford). 52(Suppl. 3):52-55, 1976.

The need for more precise definition of tricyclic antidepressants in order to use them to their best advantage in treating affective disorders is discussed. In particular, those compounds of true tricyclic structure appear to be effective in treating endogenous depression if they also inhibit amine membrane pump action. Many points still remain, however, to be clarified. Psychiatrists and general practitioners are urgently in need of more specific information in light of recent extention of tricyclics to include such compounds as iprindole and maprotiline. Comment on these observations is included, focusing on the validity of the biogenic amine theory of affective disorders and the relative effectiveness of various members of the current tricyclic drug family in relation to this theory, the question of presynaptic receptor blockade, the activity of dopamine receptors in the CNS, evidence of delay before the clinical effect is manifest following administration of an antidepressant, and drug side-effects in treating depression. 17 references. (Author abstract modified)

000662 Viukari, N. M. A.; Jaaskelainen, J. Department of Psychiatry, University of Helsinski, SF-00180 Helsinki 18, Finland **Do tricyclic antidepressants work?** Lancet (London). 1(7971):1240, 1976.

The nature of the therapeutic response to the tricyclic antidepressants i.e.,phenobarbiton, benzodiazepines, and neuroleptics is examined. In contrast to the argument of Drs. Coppen and Ghose that tricyclics do not create therapeutic effects through drowsiness, the stimulation and sedation seen can be attributed to the sympathomimetic rebound effect and to increased metabolism of dopamine in the brain induced by the adrenolytic neuroleptics. Powerful rebound reactions and phase shifts are also possibilities. In addition, the effiacy of flupenthixol in treating 215 patients with anxiety, depression, and asthenia in a Norwegian double blind multicenter study suggests flupenthixol as the drug of choice for general practitioners in such cases.

000663 Vogel, H. P.; Bente, D.; Feder, J.; Helmchen, H.; Muller-Oerlinghausen, B.; Bohacek, N.; Mihovilovic, M.; Brandli, A.; Fleischhauer, J.; Walcher, W. Psychiatrische Klinik der Freien Universitat Berlin, Nussbaumallee 36, 1 Berlin 19, Germany **Mianserin versus amitriptyline: a double-blind trial evaluated by the AMP system.** International Pharmacopsychiatry (Basel). 11(1):25-31, 1976.

Amitriptyline and mianserin (GB94, a new tetracyclic with central effects) were compared in a double-blind trial. Most of the depressive symptoms were influenced by both drugs, though quantitative and qualitative differences became evident. Amitriptyline predominantly influenced anxiety, despair and suicidal tendencies, while mianserin was particularly effective in psychomotor inhibition and the reduction of vegetative complaints. Mianserin did not show anticholinergic side-effects. 6 references. (Author abstract modified)

000664 von Knorring, Lars. Department of Psychiatry, Umea University S-901 85, Umea, Sweden **Experimentally induced pain in patients with and without pharmacological treatment -- a methodological aspect.** Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(5):357-363, 1975.

The effects of experimentally induced pain in depressed patients are studied. Pain measures (PM) were made on 31 patients without, and 19 with pharmacological treatment. The patients showed mild to severe depressive syndromes. The drugs used were tricyclic antidepressants and minor or major tranquilizers in small doses. Electric stimulation applied to the hands via saline electrodes was used. No significant difference in PM was found among the patients, regardless of sex, age or depth of depression. Nor was there any difference in PM between those patients with and those without pharmacological treatment. The lack of difference may be explained by the relatively small dosages involved and the short duration of treatment. 11 references.

000665 Waldmeir, P. C.; Greengrass, P. M.; Baumann, P.; Maitre, L. CIBA-GEIGY Limited, Basel, Switzerland **Effects of clomipramine and other tricyclic antidepressants on biogenic amine uptake and turnover.** Postgraduate Medical Journal (Oxford). (Suppl. 3):33-39, 1976.

The neuronal reuptake of noradrenaline and serotonin in the peripheral and central nervous systems was investigated. The relative degrees of inhibition of serotonin and noradrenaline uptake were determined for several antidepressant drugs including clomipramine and maprotiline, and a biochemical classification was attempted on the basis of the findings obtained. The inhibitory actions of some tricyclic drugs on amine uptake were shown to be reflected in a corresponding lowering of amine synthesis. A study of the effects of 4 day treatment with clomipramine and maprotiline on the uptake of serotonin into thrombocytes and on tryptophan binding in human plasma revealed that neither drug affected tryptophan binding and that only clomipramine and maprotiline appear to be the most specific inhibitors of serotonin and noradrenaline uptake respectively. 23 references. (Author abstract)

000666 Wang, Yao-Chun; Young, Y. K. Clinical Laboratories of Pharmacology and Psychiatry, Tri-Service General Hospital, Taipei, Taiwan **An evaluation of beta-adrenergic receptor function in depressed patients.** Chinese Medical Journal (Taipei). 22(3):172-179, 1975.

Beta-adrenergic receptor function was studied in 12 depressed patients (aged 26 to 42). Cyclic AMP formation in response to isoproterenol (ISO) and to ISO plus propranolol was measured in leukocytes taken from the depressed patients (both unipolar and bipolar) and control subjects. Results showed that, between the patient and the control, there were no statistical differences on the production of (3H)-cyclic AMP in mixed leukocytes after ISO stimulation. Likewise, propranolol produced a dose dependent inhibition of radioactive cyclic AMP formation in leukocytes after being stimulated by 5mM of ISO. Inhibition observed in the depressed patients also was not significantly different from that measured in the control subjects. It was concluded that the data do not support the concept of diminished beta-adrenergic responsiveness in depression, and that some decreases in central response of adenylate cyclase to catecholamine may exist in depression which may not have been detected by the study of the leukocyte system. 44 references. (Author abstract modified)

000667 Waring, E. M.; Chamberlaine, C. no address **The treatment of life threatening cardio-pulmonary illness and life threatening depressive illness: "suicide equivalents"?.** Medicina Psicosomatica (Roma). 20(4):411, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975), paper reviews the literature on treatment of depressive illness in severely ill medical patients. Inquiry was prompted by the death of two patients seen by a psychiatric consultation liaison service in a general hospital who had severe cardiopulmonary disease and severe depressive illness with suicidal features. It is concluded that use of antidepressant medication in patients with severe cardiopulmonary disease may contribute to further cardiopulmonary problems. Each of the two cases cited showed severe agitation as part of the depression, and demonstrated the "giving up, given up syndrome" of Engel. As a result of review of the two cases, a rationale was developed for treatment of severely depressed patients with life threatening cardiopulmonary illness: 1) transfer of patients from the medical ward to the psychiatric ward; 2) clear communication between all physicians responsible for the management of these patients; 3) avoidance of antidepressant medication or electroconvulsive therapy; 4) provision of psychotherapy and ventilation of feelings about the illness; and 5) family therapy. (Author abstract modified)

000668 Watanabe, Masayuki; Yokoyama, Shigeo; Kubo, Shinsuke; Iwai, Hiroyuki; Hashimoto, Michiko; Hayashi, Yasuaki; Omori, Shoichi; Somori, Atsuko. Department of Psychiatry and Neurology, Kawasaki Medical College, Kurashiki, Japan **A study of the antidepressive effect of Maprotiline.** Japanese Journal of Psychotherapy (Tokyo). 4(10):1225-1237, 1975.

The new antidepressant, maprotiline, was tested on 27 patients suffering from various forms of depression. It was administered in doses of from 30-150mg over a period of from 1-5 weeks. It was found to be very effective in seven cases, effective in six, partially effective in three, ineffective in eight, caused deterioration in two cases, and in the other case its effect was unclear. In most cases, improvement in the depression took place after 3 weeks of treatment, and it was effective against a wide spectrum of depression symptoms. Thirteen of the patients experienced side-effects of lethargy, thirst, headache, and sleepiness among the most common. No effect on kidney or the liver functions could be detected. 21 references.

000669 Widerlov, Erik; Sjostrom, Rolf. Forskningskliniken, Ullerakers sjukhus, 75017 Uppsala, Sweden **/TRH effects on endogenously depressed males./** Effekter av TRH vid endogen depression. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):503-512, 1975.

The antidepressive effects of thyrotropin releasing hormone (TRH) and concentrations of thyroid stimulating hormone (TSH) are studied. The trial was designed as a double-blind study; 10 males with primary depression were randomly allocated to two groups. One group received injections of TRH 600micrograms daily for 7 days and the other group received saline. All patients received 75mg amitriptyline daily after 4 days. The effect on depression was assessed by a self-rating "100mm-test" and by the comprehensive Psychiatric Rating Scale. Both types of ratings showed gradual improvement but no difference existed between the TRH and saline treated patients. TRH 600micrograms daily for 7 days has no therapeutic effect on endogenously depressed males. TSH concentrations as a biochemical indicator of the severity of depressions is discussed. 31 references.

000670 Yagi, Kazuichi; Kodama, Uichi. Department of Neuro-psychiatry, Kagoshima University School of Medicine, Japan **Clinical experience in using new antidepressant Maprotiline (CIBA 34, 276-Ba) against various kinds of depressive illnesses.** Medical Consultation and New Remedies (Tokyo). 12(6):1455-1463, 1975.

Results are given of a testing program for the new antidepressant, Maprotiline (CIBA 34,276-Ba). The tests were staged over a 19 month period on 30 patients suffering from various kinds of depression. The drug was administered in doses from 50 to 75mg per day. In the tests, the drug was found to be very effective in 33.3% of the cases, effective in 26.7%, partially effective in 13.3% no change in 16.7% and counterproductive in 10% of the cases. Doctors found that generally, patients taking the drug would become more active followed by improvement in their emotional stability. Thirty percent of the patients experiences some side-effects from the drug: dry throat, dizziness, blurry vision, or frequent urination. 5 references.

000671 Young, J. P. R.; Hughes, W. C.; Lader, M. H. St. Thomas's Hospital, London SE1, England **A controlled comparison of flupenthixol and amitriptyline in depressed outpatients.** British Medical Journal (London). No. 6018:1116-1118, 1976.

Sixty depressed outpatients were allocated to treatment with either amitriptyline (75-225mg/day) or flupenthixol (1.5-4.5mg/day) in flexible dosage for 6 weeks under double-blind procedures in order to test the effectiveness of flupenthixol. Various objective and subjective assessments were carried out before and after 1, 3, and 6 weeks of treatment. Twenty three patients completed the course of amitriptyline and 28 completed the course of flupenthixol. Almost all variables improved significantly over time, irrespective of drug. On most ratings there were no significant differences between the two drugs, but the trends favored flupenthixol. In particular, flupenthixol lessened anxiety scores more than amitriptyline. Unwanted effects were few and not troublesome except in two patients receiving amitriptyline. Flupenthixol, in low dosage, is a useful alternative antidepressant for depressed outpatients. 14 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

000672 Ananth, J.; Solyom, L.; Wyndowe, J. no address **Anafranil in obsessive compulsive neurosis.** Medicina Psicosomatica (Roma). 20(4):427, 1975.

A 4-week uncontrolled study with 20 obsessive-compulsive neurotic patients who were administered chlorimipramine was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Chlorimipramine has been reported by several researchers to have antiobsessional effect. It was cautioned, however, that because obsession can be a symptom of depression, it is important to ascertain whether the drug has a primary antiobsessional effect. The Mandsley personality inventory and the Leytons obsessive inventory were used to ascertain antiobsessional effect. The severity of obsession decreased significantly in 1 week, while depression improved in 2 to 3 weeks. In addition, improvement in the patient's social adjustments preceded the improvement in depression, indicating a primary antiobsessional effect of Anafranil. It is concluded that the serotoninergic property of Chloromipramine may modulate the hyperdopaminergic state of obsession. (Author abstract modified)

000673 Antonelli, F.; Di Donato, R.; Idone, F.; Pariante, F.; Saraceni, C. no address **/Experimental clinical use of pinazepam in psychosomatic medicine./** Sperimentazione clinica del Pinazepam in medicina psicosomatica. Medicina Psicosomatica (Roma). 20(3):217-232, 1975.

Effectiveness of the drug pinazepam on anxiety was tested in 100 patients of both sexes, 20 to 60 years old. The patients were suffering primarily from psychosomatic illnesses. Results were found to be positive. Pinazepam was found to act more rapidly and to last longer than other benzodiazepines: it did not cause side-effects and was well tolerated by the patients. 8 references.

000674 Bastecky, J.; Cervenki, J. no address **Psychoactive drugs in the treatment of psychosomatic disorders in gynaecology.** Medicina Psicosomatica (Roma). 20(4):331, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975), paper discusses indications and possible risks of groups of psychoactive drugs in management of various gynecologic disorders. Many gynecologic diseases are characterized by a presence of psychosomatic components. These include especially adnexitides, often leading to secondary sterility, primary sterility, irregularities of ovariel cycle, dysmenorrhoe, premenstrual tension, climacteric disorders and other hormonal disturbances and tumors. Psychotropic drugs have proved their efficiency in the treatment of these conditions. Benozodiazepines and other anxiolytics, antidepressants and some neuroleptics with antidepressant action have been mostly used together with hormonal treatment and psychotherapy. (Author abstract modified)

000675 Bianchi, A. no address **Experimental and clinical investigations on the behavioral and electrocardiographic effects of bromazepam.** Medicina Psicosomatica (Roma). 20(4):419-420, 1975.

A discussion of an experimental and clinical investigation of the behavior and electrocardiographic effects of bromazepam was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). It was noted that bromazepam, which has shown good tolerability in various species of animals and in man, in doses still ineffective on spontaneous behavior and on the electrocardiogram, exerts clearcut sedative and deconditioning effects in the guinea pig. It is concluded that in clinical trials bromasepam exhibits strong anxiolytic properties and shows a good activity in the treatment of psychosomatic disorders, especially of cardiovascular psychogenic somatopathies. The eventual cardiovascular somatic actions of bromazepam may be taken in consideration. (Author abstract modified)

000676 Brand, M.; Escher, M.; Menzl, A.; Horisberger, B. no address **/Cost/profit analysis of antidepressants./** Kosten-Nutzen-Analyse Antidepressiva. Berlin, Springer, 1975. 77 p. DM22.

A cost/profit analysis of antidepressant medications is presented. An overview of other depression treatments such as electroshock therapy compares cost/profit effectiveness with antidepressant drugs. Medical and social aspects of treatment and analysis are presented as well as basic questions such as revolving door psychiatric treatments, decentralization and humanization of the treatment program, and symptom elimination vs. problem elimination.

000677 Burrows, G. D.; Davies, B.; Fail, L.; Poynton, C.; Stevenson, H. Department of Psychiatry, University of Melbourne, Royal Melbourne Hospital, Victoria 3050, Australia **A placebo controlled trial of diazepam and oxprenolol for anxiety.** Psychopharmacology (Berlin). 50(2):177-179, 1976.

A double-blind study was carried out in which 62 patients with moderately severe anxiety symptoms were treated with either oxprenolol, diazepam or placebo. All treatment groups significantly improved during the study; however, in the third week of treatment, improvement was greater in the diazepam and oxprenolol groups. Observer preferences favored the diazepam group. Oxprenolol did not prove to be superior to diazepam in the treatment of somatic symptoms (such as palpitation) associated with anxiety. 6 references. (Author abstract modified)

000678 Cole, Johnathan O. Boston State Hospital, Boston, MA **Early clinical drug evaluation unit.** Psychopharmacology Bulletin. 12(3):77-78, 1976.

The effectiveness of various psychoactive drugs in a range of psychiatric conditions is studied in geriatric patients, patients with mixed anxiety and depression, and other psychiatric patients in a standard placebo controlled procedure. Long-acting fluphenazine (Prolixin) enanthate is reported to be superior to phenothiazine in outpatients who cannot be relied upon to self-administer medication. Paranoid patients were especially responsive to the drug. Doxepin (three times daily) proved superior to placebo in maintaining psychoneurotic outpatients; substantial improvement occurred after 1 week in symptoms of anxiety and after 4 weeks in symptoms of depression. Doxepin also improved sleeping. Single doses of doxepin at bedtime appear to be as effective as three times daily administration. Hydroxyzine and lorazipan have a slow onset of action; significant improvement in symptoms of anxiety neurosis occur only after 4 weeks of medication. Demographic variables as predictors of drug responsiveness revealed a correlation between socioeconomic level and response. The higher a patient's socioeconomic level, the better the response. No predictions could be made on the basis of other variables including sex, age, marital status or duration of illness.

000679 D'Amico, N.; Arrotta, M.; Greco, N.; Nania, A.; Santacroce, P. Ospedale Civile Regionale A. Pugliese, Catanzaro,

Italy /**Use of ST 1191 in hospitalized patients.**/ Impiego dell'ST 1191 in malati lungodegenti. Rivista di Neuropsichiatria e Scienze Affini (Parma). 21(1):1-12, 1975.

A clinical test was made of the new psychotropic drug ST-1191, delta 2-1,2,4-triazoline-5-one-1,3-(4-m-chlorophenyl)-1-piperazinyl/propyl-3 4-diethylchlorhydrate with major and minor tranquilizing and antidepressant action. A total of 33 long-term hospitalized patients, including 14 males and 19 females, mostly 70-80 years old, were divided into three groups. The first group, with anxious depressive symptoms was given 100mg/day, the 2nd group, with somaticized anxious depressive syndrome, was given 100mg/day, and the 3rd group, with anxious depressive psychosomatic symptoms, received 50mg/day. The drug exhibited rapid and high effectiveness on psychoneurovegetative symptoms and certain neurological signs. Individualization of the dosage enabled avoidance of side-effects, and biological tolerance proved perfect. The physical, mental and emotional benefits achieved by ST 1191 makes it a particularly suitable drug for use in both hospitalized and outpatient geriatric subjects. 12 references.

000680 Deberdt, R. no address **Treatment of obsessional and phobic neuroses with Ro 5-3350 (Lexotan).** Medicina Psicosomatica (Roma). 20(4):419-420, 1975.

A study of the use of Ro 5-3350 (Lexotan), a new benzodiazepine with anxiolytic properties, in obsessive and phobic neuroses was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Lexotan was compared with Valium in an open study and then in a double-blind study following two different grouping techniques. It is concluded that in equal doses, Lexotan appears to give better results than Valium. (Author abstract modified)

000681 Easton, J. Donald; Sherman, David G. Dept. of Medicine, Southern Illinois University School of Medicine, Div. of Neurology, P.O. Box 3926, Springfield, IL 62708 **Somatic anxiety attacks and propranolol.** Archives of Neurology. 33(10):689-691, 1976.

While patients with acute anxiety like attacks are often evaluated for various medical conditions, and, when nothing is found, their symptoms are attributed to psychogenic causes it is suggested that "B-adrenergic hyperactivity" be considered. Six patients are described who seem to be suffering from this condition. Low rates of isoproterenol hydrochloride infusion precipitated symptoms that mimicked their spontaneous somatic anxiety attacks. Treatment with propranolol hydrochloride produced long-term symptomatic relief. 14 references. (Author abstract)

000682 Fabre, Louis F., Jr. University of Texas Medical School, Houston, TX **Pilot open label study with alprazolam (U31,889) in outpatients with neurotic depression.** Current Therapeutic Research. 19(6):661-668, 1976.

Sixteen outpatients diagnosed as suffering from depressive neurosis were treated with alprazolam, a new benzodiazepine of the triazolobenzodiazepine class, for 21 days in an open label study. Moderate to marked improvement was noted in 80 percent of patients. By analysis of variance, significant improvement in all physician ratings (Abbreviated Hamilton Depression Scale, Therapeutic Effect and Target Symptoms) as well as patients evaluations (Self-Rating Scale and Patients Global Impression). Only one patient was terminated because of side effects. These results suggest that alprazolam would be an effective single medication in treatment of anxiety and depression. 15 references. (Author abstract modified)

000683 Faleni, A. no address /**Clinical evaluation of the antidepressant action of Trazodone: observations in psychogeriatrics.**/ Valoracion clinica de la actividad antidepresiva de Trazodone -- sus indicaciones en psicogeriatria. Medicina Psicosomatica (Roma). 20(4):417, 1975.

The use of Trazodone in single-blind studies was examined at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). A group of 30 male and female psychiatric patients, 24 to 86 years of age, received Trazodone for 6 weeks. In 80% of the cases favorable results were achieved, which is of a special interest in geriatric patients, who must be limited in dosage. The thymoanaleptic effect of the drug became evident between the 3rd and and 6th weeks of the clinical trial. Trazodone showed no evidence of parkinsonism, no adverse effect on the central respiratory system, and shows no cardiotoxic signs.

000684 Feldman, L. 76 Westbury Street, East St. Kilda, Victoria 3183, Australia **Treatment of nightmares.** Medical Journal of Australia (Glebe). 1(14):504, 1976.

Doses of 80 to 160mg of propranolol or oxpranolol given to patients suffering from nightmares were found effective in preventing nightmares and improving general well-being. It is proposed that sympathetic neuronal activity, stimulated by bad memories, increases during sleep and causes release of catecholamines which have free access to beta-receptors. When the stimulus reaches a level above the sleep threshold the person awakes, terminating the release of catecholamines and the normal state is returned to. It is concluded that a small dose of a beta-adrenoreceptor antagonist is apparently sufficient to antagonize the action of catecholamines by blocking the stimulations of the beta-adrenoreceptors during sleep.

000685 Foster, Thomas Warren. Ohio State University, Columbus, OH 43210 **Drug therapy for sociopathic offenders: an experimental treatment program utilizing imipramine hydrochloride. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-9968 HC$15.00 MF$8.50 328 p.

Drug therapy for imprisoned sociopathic offenders was studied, focusing on the effects of an antidepressant drug (imipramine hydrochloride) on the symptomatology and behavior of psychiatrically diagnosed simple sociopathic subjects as compared to that of nonsociopathic imprisoned controls. It was found that the simple sociopaths showed significantly greater improvement during treatment with imipramine than controls. They reported fewer adverse physical side-effects during therapy, increased energy, greater alertness, improved appetite and other evidence of subjective improvement. Most controls reported either no change or a worsening of their subjective conditions. Clinical observations and behavioral measures substantiated the subjects' self-reports, as did the psychometric tests. The findings suggest that some sociopaths experience general psychophysiological improvement in response to imipramine therapy and lend some support to the theory that simple sociopathy is a disorder of psychophysiologic hypoarousal and, as such, in amenable to drug treatment at least for symptomatic relief. (Journal abstract modified)

000686 Freed, G. no address **Therapeutic amelioration of anxiety related hypertension and angina pectoris.** Medicina Psicosomatica (Roma). 20(4):393-394, 1975.

Subjects with severe phobic anxiety, depression, hypertension and angina pectoris were discussed at the Third Congress

of the International College of Psychosomatic Medicine (Rome, September, 1975). Thirty eight patients, 36 to 49 years old, were given specific phenothiazine and monoamine oxidase inhibiting medication with the aim of obtaining anxiolytic, antidepressant and antihypertensive effects. Lowering of blood pressure levels is discussed in conjunction with heightened euphoria and implications of paradoxical reversal of expected pressor effects. Outpatient psychotherapeutic followup through individual and group psychotherapies, together with ongoing monitoring of anxiety and hypertensive parameters, was highlighted. (Author abstract modified)

000687 Fukuda, Kazuhiko; Morifuji, Toshikuni; Ishii, Atsushi. Department of Neuropsychiatry, Tohoku Medical School, Tohoku, Japan **Changing therapy and prognosis in manic-depressives.** Psychiatra et Neurologia Japonica (Tokyo). 77(7):523-524, 1975.

A followup study of some of the 1214 patients who were suffering from depression, mania, and manic-depression during the period 1955-1965 is presented. These patients were treated with drugs and/or electroshock therapy. Of 69 hospitalized depressed patients, 84% were released within 3 months after both treatments, while 24% of outpatients required prolonged drug therapy from 4 to 29 months. Among the manias and those who were manic-depressive, the combined use of both therapies lasted only 3 months in 78% of the cases, while sole use of drug therapy took much longer. In fact, 86% required treatment for 5 to 15 years. Since this was the period of time when electroshock therapy was gradually being supplanted by drug therapy it is suggested that the results of the two should be thoroughly debated.

000688 Gabrielli, F. no address **Compulsive water-drinking during depressive reaction.** Medicina Psicosomatica (Roma). 20(4):395, 1975.

A case of compulsive water drinking (up to 4 liters/day), marked drowsiness, retarded depression, complaint of fatigue and impairment of vision was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Differential diagnosis of organic brain syndrome associated with intracranial neoplasm, diabetes insipidus, psychogenic polydipsia, and water addiction had to be considered. Antidepressant drugs reassured both therapist and patient until a psychotherapeutic approach developed and cleared mood disturbances and the psychodynamic meaning of the abnormal water drinking. (Author abstract modified)

000689 Guantieri, G.; Di Donato, R.; Diodato, S. no address **Clinical experiences with ipotalamine in psychosomatic gastrointestinal syndromes.** Medicina Psicosomatica (Roma). 20(4):425, 1975.

A report of clinical experiences with ipotalamine in psychosomatic gastrointestinal syndromes was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). It was noted that it seems probable that hypothalamic phospholipid fractions exert a positive influence on psychosomatic syndrome correleated with a dysfunction occurring in the hypothalamic limbic system. According to this hypothesis, and because of the tight correlations between the vegetoemotive and psychodynamic aspects of man, the preparation containing hypothalamic phospholipid fractions corresponding to 400 gamma of lipidic P (Ipotalamine) was administered to subjects suffering from psychosomatic gastrointestinal systems to observe effect on emotions, and/or psychosomatic symptoms. (Author abstract modified)

000690 Herceg, Neda. 367B Crown Street, Wollongong, New South Wales, 2500 **Successful use of thiothixene in two cases of pathological jealousy.** Medical Journal of Australia (Glebe). 1(16):569-570, 1976.

Two case histories of pathological jealousy are reported demonstrating successful use of thiothixene without the incidence of typical extrapyramidal symptoms. Alcoholism played no part in the etiology of the disease in these patients who were treated on an outpatient basis. The projection mechanism in delusional jealousy is reviewed and evaluated. 11 references.

000691 Holmgren, Sven. AB Volvo-Flygmotor, Trollhattan, Sweden **Pimozide in the treatment of stressinduced psychic and functional disorders: a double-blind comparison with chlopoxide and placebo.** Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(7):577-584, 1975.

Pimozide is used as a psychic stabilizer as an alternative to benzodiazepine derivatives. In order to study its effects, 16 skilled workers were selected. They all presented symptoms of neurasthenic insufficiency and/or vegetative neurosis. The duration of treatment was 2 weeks. The dosage was 1mg daily during the first week and 2mg daily during the second week. A double-blind three way crossover design was used in a control study. Pimozide, chlopozide and placebo were presented in identical capsules. Both pimozide and chlopozide had a significantly better effect than the placebo. A double-blind crossover comparison of the two drugs on 50 patients was also made. No differences were found between the results. The study shows a positive effect in the treatment of stress induced psychic and functional disorders. Since the drug treatment is needed for a long time, the drug prescribed should lack addiction potential. 12 references.

000692 Kimura, M.; Nakagawa, T.; Ikemi, Y.; Suehiro, K.; Ito, H. no address **Psychopharmacological study on the depressive state in medical practice.** Medicina Psicosomatica (Roma). 20(4):303, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975), paper reports a study which evaluated the efficacy of antidepressants by administering doxepin and imipramine to 191 depressive patients of internist practitioners for 6 weeks. No significant difference was found between the two drugs regarding general improvement rating and side-effects. It was concluded that imipramine was more effective in endogenous dopression, and dexepin was better in neurotic depression. No difference was found, however, in involutional depression. The depressive patients were given the Microvibration Test (MV). Neurotic patients tended to show normal patterns, while significantly more patients with endogenous and involutional depressions showed abnormal patterns. It was observed also that MV patterns changed in accordance with the treatment process of depression. The relationship between MV patterns and diurnal variations of the depressive state were examined and a marked correlation was found between them. In many depressive patients, abnormally high levels of blood sugar were observed at the onset and recurrence of depression. (Author abstract modified)

000693 Lamontagne, Y.; Pinard, G.; Lavalle, Y.; Tetreault, L.; Annable, L. no address **Therapeutic efficacy of EMG feedback and its interaction with diazepam in chronic anxiety.** Medicina Psicosomatica (Roma). 20(4):285, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September 1975), paper presents a study of 40 patients with chronic free floating anxiety, who were randomly assigned to one of four groups in a classic interaction design: 10 patients received EMG feedback and diazepam, 10 EMG feedback and diazepam placebo, 10 EMG feedback placebo and diazepam and 10 both placebo. It is concluded that a definite effect of combined treatment on the physiological measurements of anxiety is indicated. However, dissociation of these measures and psychological self-evaluation seems to exist in the chronic anxious patient. It is concluded also, that this study underlines the importance of rigid scientific experimental designs to evaluate the efficacy of any new treatment in psychiatry. (Author abstract modified)

000694 Mahal, A. S.; Malik, S. C.; Srinivasamurthy, Usha. National Institute of Mental Health and Neurosciences, Bangalore 560 027, India **Evaluation of loxapine succinate as an anxiolytic in comparison with chlordiazepoxide.** Current Therapeutic Research. 20(1):84-93, 1976.

The therapeutic effects of loxapine succinate were compared with those of chlordiazepoxide in a double-blind study involving 60 patients with anxiety. Dosages of both drugs were adjusted according to the patient's response and/or the appearance of limiting side-effects. Assessment was done weekly for 4 weeks. Both drugs are reported to be equally effective. Minor side-effects which did not necessitate interruption of treatment were observed in both treatment groups. 6 references. (Author abstract modified)

000695 Marks, Isaac. MRC Unit, Institute of Psychiatry, London, England **Studies on the combined use of diazepam with exposure in vivo.** Bulletin of the British Psychological Society (London). 28:243-244, 1975.

Studies on the combined use of diazepam with exposure in vivo in treating neuroses are reviewed, emphasizing that when drugs and psychological treatments are used together for psychiatric disorders, their interaction with one another may lead to separate effects and that controlled research data are scanty. In phobias, tricyclics and monoamine oxidaze inhibitors have been of significant benefit compared to placebo, the effect not being of an antidepressant kind. During exposure in vivo beta-adrenergic blockers have reduced autonomic symptoms in phobics more than placebo, though avoidance was not affected. One double-blind study in specific phobics of oral diazepam during individual exposure in vivo found that fear was reduced significantly more after exposure was given during its waning psychotropic phase than after placebo. Exposure during the peak psychotropic phase was intermediate. There was no evidence of state dependence at this moderate dosage (0.1mg/kl) and no relationship between outcome of blood level of diazepam, which varied greatly between individuals but was constant for the same individuals over different occasions, occurred. Subjective anxiety was similar during exposure with or without diazepam. In a different design another double-blind study examined exposure in vivo of agoraphobics during waning and peak phases of diazepam and placebo. Patients on diazepam showed significantly less subjective discomfort than did placebo patients during exposure in vivo. However, overall decrease in phobias was similar in each treatment. There was no evidence that 0.1mg/kl of diazepam impaired improvement in either the waning or peak phase. (Author abstract modified)

000696 Ohkuma, Teruo; Kishimoto, Akira; Matsujima, Yoshihiko; Orgura, Chikara; Fukuma, Etsuo. Department of Neuropsychiary, Tohoku University, Tohoku, Japan **The therapeutic and preventative effects of carbamazepine (tegretol) on depression.** Psychiatria et Neurologia Japonica (Tokyo). 77(7):523, 1975.

The effects of the drug carbamazepine (tegretol), both as an antidepressant and as a depression preventative are reported for a relatively large number of patients over a long period of time. The daily dosage of carbamazepine was from 200 to 1200mg (average dose: 400-600mg), with the majority of the patients taking it in addition to the antidepressant they were currently using. Of the 61 depressed patients, 16% showed marked improvements, it was effective in 16%, slightly effective in 21%, there was no change in 51%, and the condition deteriorated in 2% of the patients. As a preventative, out of 51 persons, the drug was very effective in 35%, effective in 32% and there was no change 33% of the cases. As a depression preventative, the effects of the drug were far better than as a treatment. Side effects similar to those when the drug is administered for epilepsy were seen in 21% of the cases.

000697 Okada, Fumihiko; Kimura, Naoki; Miyagishi, Tsutomu; Takahata, Naohiko; Yamashita, Kaku; Suwa, Nozomi. Department of Psychiatry and Neurology, Hokkaido University Hospital, Sapporo, Japan **Clinical experience of a new tranquilizer, N-demethyl diazepam (A 101) -- for neuroses.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(12):1509-1518, 1975.

The tranquilizer, N-demethyl diazepam (A 101), which has been widely reported to relieve anxiety through its hypnotic action, was tested on 30 outpatient neurotics ranging in age from 17 to 65. Daily dosage of the drug was from 6-17mg, with treatment administered for 2 days to 20 weeks. For each patient, age, sex, period of illness, diagnosis, major symptoms, dosage, period of use, notation of any other medications being used, effect of the drug, and any side-effects are listed. General results indicate that the drug was at least somewhat effective in 70% of the cases (very effective in 2 cases, effective in 11, somewhat effective in 8, ineffective in 7, and detrimental in 2 cases). Side-effects were noted in four cases; two patients showed inability to focus eyes, sleepiness, and the other two patients, who were taking amitriptyline and nitrazepam, became intoxicated and had trouble walking. Those who showed side-effects were taken off the drug. No abnormalities in metabolic functions could be detected in the patients taking N-demethyl diazepam. 7 references.

000698 Pach, J.; Waniek, W. Rheinische Landes- und Hochschulklinik fur Psychiatrie Essen, Hufelandstrasse 55, D-43 Essen 1, Germany /**Comparative study of the tranquilizer effect of fluspirilene and diazepam.**/ Vergleichende Untersuchung zum Tranquilizereffekt von Fluspirilene und Diazepam. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(2):61-66, 1976.

Fluspirilene and diazepam were compared in an 8 week crossover study on 34 patients with functional organic diseases, depressive anxiety, and vegatative irritability, 28 of whom completed the study, including 12 males and 16 females, mean age 32 years. Patients received either 5mg diazepam t.i.d. with a weekly injection of NaCl solution or a placebo tablet t.i.d.,and a weekly injection of 1.5mg fluspirilene. All patients completed the Freiburger Personality Inventory, the Self-Rating of Mood Scale, and a list of symptoms. Both medications were effective against somatic disorders, anxiety, and depression. Fluspirilene proved to be more mood elevating and more activating, without being hypnotic. The indications for both drugs are discussed, emphasizing the therapeutic perspectives of the new long-acting tranquilizer. 15 references.

000699 Perez De Francisco, C. no address **Preliminary open study of nomifensin: a new antidepressant.** Medicina Psicosomatica (Roma). 20(4):402, 1975.

Use of Nomifensin on 18 depressive patients was reported at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). All patients were depressed (endogenous or not) and chronic. All but one were treated for more than a month with a dosage of 25 to 150mg/day. Six patients showed excellent results eight showed good improvement, three remained clinically unchanged, and one had to stop treatment because of strong tachycardia and marked general discomfort. It was concluded that except for small inconveniences, such as dryness of the mouth, slight constipation, and asthenia, there were no important side-effects, except in two cases. Therapeutic effects were remarkable and rapidly noticeable in most cases. No pharmacological incompatibilities were found with other psychotropic drugs given concommitantly. (Author abstract modified)

000700 Pisana, F. Servizio Provinciale di Neuro-Psichiatria ed Igiene Mentale, Amministrazione Provinciale Regionale di Ragusa, Italy **/Controlled clinical experiment with a new preparation of dipotassium chlorazepate with delayed action./** Considerazioni sulla sperimentazione clinica controllata di un nuovo preparato di clorazepato dipotassico ad azione ritardo. Rivista di Neuropsichiatria e Scienze Affini (Parma) 21(1):13-23, 1975.

A controlled study was made of the drug FM-3473 Retard (dipotassium chlorazepate) in 25 males and 25 females, 20-87 years of age, with various forms of acute anxiety. For 2 weeks half the patients received one tablet of 22.5mg/day, and the other half received three tablets of 7.5mg/day. Results showed effective anxiolytic action, but no significant difference was noted between the two forms of administration, permitting the conclusion that FM-3473 has great advantages for outpatient treatment. 10 references.

000701 Poldinger, W. Kant. Psychiatrische Klinik Wil, CH-9500 Wil, Switzerland **Application of the neuroleptic pimozide (ORAP-R 6238) for tranquilizer indications in a controlled study.** International Pharmacopsychiatry (Basel). 11(1):16-24, 1976.

The effect of the neuroleptic pimozide the first diphenylbutyl piperidine derivative at doses of 2mg/day was compared with that of diazepam at doses of 3x5mg. This double-blind study involved 50 outpatients with psychovegetative syndromes and anxiety neuroses. At these doses and under the described test conditions both preparations were virtually equally effective. Pimozide can therefore be considered an alternative preparation for 'genuine' tranquilizers. Above all, its application seems to be useful in patients that are prone to drug abuse, and therefore, a priori, endangered by habit formation. 7 references. (Author abstract)

000702 Quillien, R.; Patay, M. Hopital Psychiatrique, Service du Dr. Mahe, F-29210 Morlaix, France **/Various aspects of high doses of potassium chlorazepate and certain neuroleptics on psychomotor tolerance./** Quelques aspects de la tolerance psycho-motrice de fortes doses de clorazepate dipotassique et de certains neuroleptiques. Psychologie Medical (Paris). 8(3):475-479, 1976.

The effects of high doses of potassium chlorazepate (average daily dose 120mg) or neuroleptic sedatives upon psychomotor tasks are studied in two groups (total n=240) of anxious/neurotic patients. Results confirm the better tolerance of benzodiazepine. 2 references. (Journal abstract modified)

000703 Riva, D.; Lampugnani, E.; Matteoli, E. no address **Cardiac neurosis: treatment with a new benzodiazepine (Lexotan).** Medicina Psicosomatica (Roma). 20(4):421, 1975.

A study of the personality of cardiac neurosis patients was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). It was noted that the anxious state, often associated with hysterical or obsessive features, scarce quickness of wit, self-centeredness, and difficulty in having good social relations, often characterizes the personality of these patients. A controlled trial with Bromazepam (Lexotan) was undertaken. It is concluded that the drug positively affects the cardiovascular symptomatology as well as the anxious state of the patients. (Author abstract modified)

000704 Rybakowski, Janusz; Strzyzewski, Wlodzimierg. Department of Psychiatry, Academy of Medicine, 60-572 Poznan, Poland **Red-blood-cell lithium index and long-term maintenance treatment.** The Lancet (London). I(7974):1408-1409, 1976.

A letter reports inconsistent data in the clinical state as a possible factor in alterations of the red blood cell (RBC) lithium index. The data include 45 patients (14 male, 31 female) with manic-depressive (bipolar) psychosis receiving lithium for 1-5 years in a manner similar to Mendels. Calculations for each patient was the mean of between 5 and 20 estimations of RBC lithium index. The results are shown in terms of responders, nonresponders, males, females, and totals, in values of plus or minus S. E. M. The investigation disclosed no difference in RBC lithium index between responders and nonresponderes. Conclusion states further investigation is needed to determine if high RBC lithium indices are significant on clinical, genetic or biochemical grounds. 10 references.

000705 Saarma, J.; Mehilane, L.; Saarma, M.; Aadamsco, A.; Lepp, H. no address **Clinical and experimental study on Trazodone.** Medicina Psicosomatica (Roma). 20(4):416, 1975.

A complex experimental and clinical study on the action and efficacy of the psychotropic compound Trazodone was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). The action of Trazodone on various effects brought about by stimulation and/or destruction of different limbic structures was investigated in rats, showing a specific pattern of antiaggressant action. The action of Trazodone on sodium ion, potassium ion and ATPase was studied in vivo and in vitro and compared with effects caused by neuroleptics and some other antidepressants. A clinical and conditioned study, including application of different rating scale and of the Tartu Psychometric Test Battery, was carried out in a sample of depressive patients: in one group Trazodone was administered orally, and in the other group intravenous infusion was applied. It is concluded that a comparatively high therapeutic efficacy of Trazodone in depressive states was obtained. (Author abstract modified)

000706 Sarteschi, P.; Valzelli, L. Istituto di Clinica Psichiatrica dell'Universita di Pisa, Pisa, Italy **/Clinicobiological observations on anxiety/.** Considerazioni clinico-biologiche in tema di ansia. Rassegna di Studi Psichiatrici (Siena). 65(2):221-231, 1976.

Anxiety is discussed in the context of biological factors as well as of emotional and affective behavior. It corresponds to a state of uncertainty rather than to one of fear, and is a component of several psychopathological syndromes, such as neuroses, psychoses, and cerebral syndromes. Anxiety therapy encompasses dialogue with the physician, group and

behavioral therapy, and psychopharmacology with groups of drugs such as the benzodiazepines. 23 references.

000707 Schneyer, Jerome J.; Goodman, Lowell I.; Borgen, Lowell A. Clinical Research Department, Parke, Davis and Co., Ann Arbor MI **Ripazepam (CI-683) double-blind comparison with placebo in anxious patients.** Journal of Clinical Pharmacology. 16(7):377-383, 1976.

An investigation was carried out to determine: 1) the anxiolytic effects of low dose (40mg/day) and high dose (80mg/day) regimens of ripazepam in comparison with placebo; 2) the overt adverse effects of ripazepam at these doses; 3) the safety of ripazepam measured at these doses as by laboratory data. Thirty anxious, neurotic patients were treated in a general practice setting with single-blind placebo for 1 week followed by 2 weeks of double-blind treatment with either placebo or 40mg/day or 80mg/day of ripazepam (CI-683). As rated by both physician and patient, ripazepam is significantly superior to placebo at both dosage levels. There is evidence that 80mg/day of ripazepam produces greater improvement than 40mg/day of ripazepam. In addition to the predicted effect on anxiety symptoms, ripazepam produces significant improvement in depression, somatization, obsessive compulsivity and interpersonal sensitivity, suggesting that the drug has a wider spectrum of psychopharmacologic activity than was anticipated. No significant changes in laboratory tests of hematopoietic, cardiac, renal or hepatic function are reported. Cardiac rate decreases significantly during ripazepam therapy but blood pressure is not changed. Vertigo and nausea are the only side-effects reported by four patients. Ripazepam appears to be a safe drug producing relatively few side-effects with little evidence of the sedative properties common to the marketed benzodiazepines. 6 references.

000708 Schonecke, O. W.; Schueffel, W. no address **Lexotanil (Ro 5-3350) in the psychosomatic treatment of patients with functional abdominal disorders.** Medicina Psicosomatica (Roma). 20(4):421, 1975.

A study of 78 patients with various functional abdominal complaints who were treated in a completely random 2 x 2 double-blind pattern with Lexotanil (Ro 5-3350) was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September 1975). Results showed that considerable improvement must be ascribed to an overall placebo effect, most probably due to properties of the treatment arrangment. It is concluded that some of the results showing an interaction between psychotherapy and Lexotanil suggest that for assessing some specific effects of a psychotropic drug, properties of the physician-patient relationship should be taken into account. (Author abstract modified)

000709 Silbermann, R. M.; Beenen, F.; de Jong, H. no address **Clinical treatment of post partum delirium with perfenazine and lithium carbonate.** Psychiatria Clinica (Basel). 8(6):314-326, 1976.

A clinical study of postpartum delirium with perfenazine and lithium carbonate is presented. Despite the development of psychopharmaceutical therapy, postpartum delirium was difficult to treat. The patients remained psychotic for long periods and the course of the disease was capricious due to the many relapses. A comparative study of two groups, one consisting of 6 patients and the other of 13, all with a typical postpartum delirium, was carried out. The symptomatic treatment of this syndrome with a combination of perfenazine and lithium carbonate produced relatively favorable results in the clinic. For the time being, the combination of perfenazine and lithium carbonate seems to be the medication of choice. 63 references. (Journal abstract modified)

000710 Singh, A. N. no address **Benzodiazepine -- derivatives in psychosomatic disorders: a pharmacological related psychophysiological approach.** Medicina Psicosomatica (Roma). 20(4):408, 1975.

A discussion of the role of benzodiazepine in both short-term and long-term alleviation of anxiety, emotional conflict, stress, anger and fear was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). An effort was made to relate pharmacological action with psychophysiological causative factors, and emphasis is placed on the benefit of long-term maintenance therapy rather than short-term treatment. It was concluded that benzodiazepine is an attractive adjunct to psychotherapy and other modalities of treatment in psychosomatic disorders for achieving smooth and prolonged alleviation. (Author abstract modified)

000711 Sirbu, A.; Hotico, Tr.; Secareanu, Al. Clinica de psihiatrie, Cluj, Romania **/Some therapeutic aspects of obsessive phobic neurosis./** Unele aspecte terapeutice ale nevrozei obsesivo-fobice. Neurologie, Psihiatrie, Neurochirurgie (Bucuresti). 20(1):17-21, 1975.

Principal therapeutic methods applied in the treatment of obsessive phobic neuroses are reviewed. These diseases are very resistant to treatment, probably due to the background of personality peculiarities on which it develops. Properizine (Neuleptil) in combination with imipramine appears to offer the most promising treatment. Preliminary trials were conducted with six patients, who were given 30 to 120mg/day Neuleptil for 4 to 6 weeks and 75 to 150mg/day antiderpin, associated with antiparkinsonian drugs and vitamins. Results were considered very good and good in four cases, satisfactory in one, and mediocre in one. 15 references.

000712 Suzuki, Takaaki. Department of Neuro-psychiatry, Asoo Cement Iizuka Hospital, Japan **Clinical experience of N-demethyl diazepam (A-101) in the field of psychiatry.** Medical Consultation & New Remedies (Tokyo). 12(10):2339-2360, 1975.

N-demethyldiazepam (A-101) was administered clinically to 48 cases with neurosis or neurotic symptoms. It was effective in 56.3% of the cases with 89% of them experiencing some kinds of effect of the drug. In the 13 patients who were taking no other drug, the effectiveness of A-101 was 69.2%. It was especially effective in combating anxiety, oversensitiveness, depression, and tension. This drug is notable because of the rapidity of its effect, sometimes appearing the day following administration. Dosage was between 6 and 15mg. Light side-effects of uneasiness, speech difficulties, and sleepiness were noted, mostly in patients over 40. Effects of the drug was considered similar to diazepam. This drug was considered especially suitable for the aged because of its safety.

000713 Tsutsui, S.; Namba, T.; Nishida, K.; Nozawa, A.; Kato, G. no address **A comparative study on the effectiveness of sulpiride and oxazolam in the field of psychosomatic medicine.** Medicina Psicosomatica (Roma). 20(4):431, 1975.

A comparative study of the effectiveness of sulpiride and oxazolam in 44 patients (8 neuroses, 21 psychosomatic disorders, and 15 with masked depression) was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Capsules containing 50mg

sulpiride and 10mg oxazolam were determined to be equivalent doses, and three to six capsules per day of each drug were administered for three weeks. Evaluation of the 44 cases showed no significant difference between the sulpiride group and the oxazolam group, though the incidence of an excellent effect was a little higher with sulpiride than with oxazolam. In comparison of the degree of improvement in symptoms, it was concluded that the rate of disappearance of anxiety, lassitude, diurnal variation and restlessness was significantly higher in the sulpiride group, while remission of headache was higher in the oxazolam group. There was no significant difference in other symptoms. Side-effects were observed in one case in the sulpiride group and four cases in the oxazolam group. No particular side-effects were observed, and both drugs showed almost the same degree of efficiency and safety. (Author abstract modified)

000714 Turner, Paul. Department of Clinical Pharmacology, St. Bartholomew's Hospital, London EC1A7BE **Beta-adrenoceptor blockade in hyperthyroidism and anxiety.** Proceedings of the Royal Society of Medicine (London). 69(5):375-377, 1976.

The relationship between adrenergic activity and hyperthyroidism and anxiety, and some therapeutic considerations of their relationship are considered. Turner's work in seeking significant dose response relationships between various beta-adrenoceptor blocking drugs on hyperthyroid tachycardia is reviewed. Increased sensitivity to adrenoceptor stimulation when drugs possessing significant partial agonist or intrinsic sympathomimetic activity are used makes alprenolol, oxprenolol, pindolol, and practolol less effective than propranolol, sotalol, and R03-3528. Experimental studies suggest that although classification of anxiety states is difficult because of central nervous system and somatic symptoms, a combination of a centrally acting drug, such as benzodiazepine, in small dosage with a beta-adrenoceptor blocking drug should produce maximum therapeutic management of these conditions. 26 references.

000715 Tyrer, Peter. University of Southampton, South Academic Block, Southampton General Hospital, Tremona Road, Southampton S09 4XY, England **Towards rational therapy with monoamine oxidase inhibitors.** British Journal of Psychiatry (London). 128:354-360, 1976.

A rational approach to the use of monoamine oxidase inhibitors (MAOIs) is outlined. Patients suitable for treatment cannot be classified adequately using conventional diagnostic labels. They include those with primary symptoms of hypochondriasis, agoraphobia and social phobias, irritability, somatic anxiety and anergia; those with primary depressed mood, guilt, ideas of reference and personality disorders seldom respond. There is great variation in the interval between the first administration of these drugs and clinical response, and this may account for the inconsistencies in published trials. The type of drug and its dose may affect rate of response, as may biochemical factors, including acetylator and monoamine oxidase status. To obtain maximum benefit, a course of therapy with MAOIs should last for several months. 61 references. (Author abstract)

000716 Van Coller, P. no address **Anxiety and tension and betablockers in ischaemic heart disease.** Medicina Psicosomatica (Roma). 20(4):410, 1975.

A study of 150 ambulant ischemic heart disease patients with a high percentage of anxiety and tension was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). The study revealed that using different beta-blockers, each as a double-blind crossover, and using the same battery of psychosomatic tests for anxiety and tension, beta-blockers with pahrmacological anxiolytic properties resulted in a dramatic drop in anxiety and tension. It is concluded that beta-blockers with anxiolytic properties are beneficial in reducing anxiety and tension in ischemic heart disease. (Author abstract modified)

000717 Wheatley, D. no address **Circulatory manifestations of soma and psyche.** Medicina Psicosomatica (Roma). 20(4):328-329, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975), paper discusses the incidence of psychiatric symptomatology in hypertension and the use of antianxiety drugs in the treatment of the condition. Many similarities between the symptoms of cardiovascular disease and affective disorders are noted, particularly when anxiety is predominant. There is further analogy between anxiety provoking situations and the physiological response to stress. (Author abstract modified)

000718 Wheatley, D. no address **Treatment of the depressed patient in the home.** Medicina Psicosomatica (Roma). 20(4):431, 1975.

A discussion of the treatment of the depressed patient in the home was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). It was noted that there are important differences between treatment of the depressed patient in the home and similar treatment administered in a hospital. The majority of cases of depression treated by the family physician are of a milder type than the severe forms of endogenous depressions seen in hospitals. Practical problems may arise when patients continue to work or carry on normal activities in the home. Relatively minor side-effects may assume considerable importance, such as dry mouth when using the telephone, or drowsiness when driving an automobile. Patients are unsupervised, and drugs with long duration of action and in a convenient form of administration are more likely to ensure effective therapy. Non-drug variables that may influence the outcome of treatment are more important when treating the patient at home, such as good or bad life events occurring during the course of treatment, which may profoundly influence response to antidepressant medication. (Author abstract modified)

000719 Wheatley, David. no address **Evaluation of trazodone in the treatment of anxiety.** Current Therapeutic Research. 20(1):74-83, 1976.

The efficacy of trazodone was compared with that of chlordiazepoxide in a double-blind study involving 83 patients with anxiety. Trazodone is highly effective in relieving anxiety symptoms. However, there are no significant differences from the response achieved with lesser dosages of chlordiazepoxide. There were no statistically significant differences in the incidence or severity of side-effects between the drugs. 15 references. (Author abstract modified)

000720 Winstead, D. K.; Lawson, T.; Abbott, D. no address **Diazepam use in military sick call.** Medicina Psicosomatica (Roma). 20(4):431-432, 1975.

A study evaluating the underlying psychological factors of patients prescribed diazepam in a general medical outpatient setting (military sick call) was discussed at the Third Congress of the Interntaional College of Psychosomatic Medicine

(Rome, September, 1975). It was noted that the popularity of diazepam is due to its use in treating the many manifestations of anxiety as seen in virtually every medical and psychiatric diagnostic category. This is confirmed by MMPI results that show the diazepam group to be more anxious and more apt to somaticize their difficulties. Diazepam is initially an effective medication in the treatment of these difficult patients, but further counseling or psychiatric consultation may be required in long-term management. It is concluded that diazepam should be judiciously prescribed for a brief period until counseling reduces the patient's anxiety. Chronic reliance on this medication should be discouraged. (Athor abstract modified)

000721 Yaryura-Tobias, J. A.; Neziroglu, F.; Bergman, L. no address **Chlorimipramine, its clinical actions.** Medicina Psicosomatica (Roma). 20(4):432, 1975.

A double-blind study of the effects of chlorimipramine on 50 patients exhibiting obsessive-compulsive syndrome was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September 1975). The study showed a clinical reduction of obsessive-compulsive symptoms and relief of anxiety and depression. It is concluded that although chlorimipramine is mostly utilized as an antidepressant, its antiobsessive-compulsive properties should not be underestimated. (Author abstract modified)

000722 Zerbi, F.; Fenoglio, L.; Tosca, P. Clinica delle malattie nervose e mentali dell'Universita di Pavia, Pavia, Italy **Plasma and erythrocyte concentrations of lithium.** Psychiatria Clinica (Basel). 8(5):236-242, 1975.

The clinical response, EMG, and EEG changes in 12 depressed patients after 28 days of lithium carbonate treatment, 1200mg/day, were evaluated. Of the patients, 9 showed unipolar depression and 3 were involutive with one or more episodes. Results showed: 1) a high correlation between the degree of improvement and the red blood cell/plasma lithium ratio on the 28th day; 2) a slight decrease in motor conduction velocity (m.c.v.)and increase of M-response duration during lithium treatment; 3) no correlation between EEG and lithium levels and percentage of improvement. 13 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

000723 Alessandri, Lucio; Fumi, Sergio; Opice, Bruno. Ospedale Psichiatrico Provinciale, S. Maria della Pieta, Rome, Italy /**Initial observations of therapeutic effects of the sodium salt of N-dipropylacetic acid.**/ Prime osservazioni sugli effetti terapeutici del sale sodico dell'acido N-Dipropilacetico. Lavoro Neuropsichiatrico (Roma). 57(1/2):299-307, 1975.

Therapeutic effect of the sodium salt of N-dipropylacetic acid on epileptics suffering from serious personality deterioration and character defects was evaluated. A group of 84 patients, 76 of whom were hospitalized, was administered the drug. Results showed that the drug does not have a tranquilizing effect of any kind; patients remained completely lucid, and behavior showed considerable improvement. Patients became less impulsive, more stable and more accessible to the influence of surroundings and of the therapists. 25 references.

000724 Antosik, Irena; Nurowska, Krystyna; Welbel, Leszek. I Klinika Psychiatryczna Instytutu Psychoneurologicznego, Al. Sobieskiego 1/9, 02-957 Warszawa, Poland /**Comparison of the therapeutic action of chloromethiazole and promazine in the treatment of geriatric psychoses.**/ Porownanie leczenia chlorometiazolem i promazyna zaburzen psychicznych wieku starczego. Psychiatria Polska (Warszawa). 10(2):147-152, 1976.

In an open crossover trial, 28 male and 2 female patients, all over 55 years of age, various psychoses, were given chloromethiazole (0.6to 3.0g daily) and promazine (50 to 300mg daily) over a period of 8 weeks. During the first 4 weeks, both drugs showed similar tranquilizing effect. After the switchover the change from chloromethiazole to promazine resulted in deterioration of the patients' mental condition, whereas the change promazine to chloromethiazole resulted in no appreciable difference in the patients' improved condition. The most serious, although not common, side-effect of chloromethiazole was an increase in secretions of the respiratory tract. It is concluded that chloromethiazole, although similar in action to promazine, is more effective in treating geriatric psychoses. 13 references. (Author abstract modified)

000725 Asam, Uta; Karrass, Wolfgang. Universitatskrankenhaus Eppendorf, Abteilung fur Kinder- und Jugendpsychiatrie, Martinistrasse 52, D-2000 Hamburg 20, West Germany /**The Gilles de la Tourette syndrome: an analysis of published cases dealing with the course of the disease and its prognosis.**/ Beitrag zum Gilles de la Tourette-Syndrom: eine Analyse veroffentlichter Kasuistiken zur Frage des Krankheitsverlaufes und der Krankheitsprognose. Zeitschrift fur Kinder- und Jugendpsychiatrie (Stuttgart). 4(1):45-54, 1976.

Gilles de la Tourette syndrome was studied on the basis of 65 cases published in German and English during the past 100 years. In 17 of the cases the course of the disease deviated from the characteristic sequence of symptoms: motor tics, explosive utterances and/or coprolalia. The prognosis is independent of age at the onset of the disease, the appearance of the symptoms and the duration of the disease prior to treatment. The prognosis is less favorable for cases with a greater number of symptoms. Definite therapeutic success was observed only in treatment with haloperidol. 54 references. (Author abstract modified)

000726 Atanasio, G.; Bisogni, A.; Dell'Unto, A. Ospedale Psichiatrico S. Niccolo, Siena, Italy /**Clinical study of the use of thiothixene in chronic psychotic patients with psychomotor inertia, depression, and autism.**/ Studio clinico sull'uso del tiotixene in pazienti psicotiche croniche con inerzia psicomotoria, depressione, autismo. Rassegna di Studi Psichiatrici (Siena). 65(4):758-770, 1976.

The effectiveness of thiothixene on depression, psychomotor inertia, and autism was tested in 20 chronic psychotic female patients, 30 to 60 years old. The test lasted a period of 60 days. Evaluations were made after 7, 20, 40, and 60 days, with the results transferred to graphs. The findings suggest that the effects of thiothixene, administered in doses of 15mg/day, were positive, and beneficial effects became evident on the 20th day. Side effects were minimal. 37 references.

000727 Augustin, P. Clinique Neurologique, Hopital Charles-Nicolle, 1, rue Germot, F-76000 Rouen, France /**Tanakan in geriatrics: clinical and psychometric study in 189 hospitalized patients.**/ Le Tanakan en geriatrie: etude clinique et psychometrique chez 189 malades d'hospice. Psychologie Medicale (Paris). 8(1):123-130, 1976.

Tanakan, an extract of Ginkgo, was given to 189 female geriatric patients, all suffering signs of arteriosclerosis. The double-blind study lasted 6 months. Patients ranged in age from 49-years-old to 95-years-old; more than half were over

the age of 76-years-old. They were randomly assigned to a placebo group (90 subjects) or a Tanakan group (99 subjects). In terms of general activity and behavior, 44 of the Tanakan patients improved and 2 got worse, whereas in the placebo group, 13 improved and 11 became worse. Psychometric tests measuring orientation, intellectual efficiency, immediate memory of figures, word learning, and visual retention were given to 168 patients at the beginning and end of the study. Improvement occurred in 61 patients receiving Tanakan and 26 patients receiving placebo, and aggravation occurred in 13 patients receiving Tanakan and 36 patients receiving placebo. No significant changes in blood pressure occurred. Arterial circulation in the lower limbs improved in 24 patients under Tanakan and 7 patients under placebo; it deteriorated in 2 patients under Tanakan and 14 patients under placebo. Pedal pulse reappeared in 8 patients under Tanakan and 1 under placebo. Six patients receiving placebo showed aggravation of atheromatous retinopathy with new exudates and hemorrhages, whereas the fundi improved in 3 patients receiving Tanakan. Eight patients receiving placebo died during the 6-month period. Tanakan was well tolerated by all patients. 17 references.

000728 Bortolotti, M.; Baruzzi, A.; Barbara, L. Clinica Medica II, Universita di Bologna, Bologna, Italy **Experimental and therapeutical effects of sulpiride on the gastric and duodenal ulcer.** Medicina Psicosomatica (Roma). 20(1):33-40, 1975.

The effect of sulpiride on gastric and duodenal ulcers was evaluated. A clinical/therapeutic study was made to examine the antiulcer effectiveness of the drug and an experimental study investigated the mechanism of drug action on gastric function. A clinical study was made of 33 ulcer patients, 25 with duodenal ulcer and 8 with gastric ulcer. The psychosomatic origin of the duodenal ulcer was established by psychodiagnostic examination based on clinical interview and a series of psychological tests. Sulpiride was administered for 30 days. Results proved good in 72% of the patients, mediocre in 12%, and absent in 16%. In the gastric ulcer cases, results were good in 75%, mediocre in 12.5%, and absent in 12.5%. An experimental study was made with 12 subjects with duodenal ulcer and 4 postvagotomy patients to study gastric motor and secretory modifications induced by sulpiride. Thirty minutes after sulpiride administration the duodenal ulcer patients showed the largest and most significant reduction in basic electric rhythm (BER) frequency and a significant rise in motility index. In the total vagotomy patients the mean BER frequency was reduced and motility increased. Conclusion was that sulpiride treatment gave good results, thus confirming other studies. The therapeutic response was similar in both the duodenal and gastric ulcer patients predominantly due to psychosomatic factors in one and local factors in the other. It was further concluded that increase in gastric acid secretion and blockage of gastric motility are produced by experimentally induced emotional conflict, and it is presumed that similar changes are involved in the genesis of the peptic ulcer. Importance of sulpiride should be stressed since it reduces gastric acid secretion and stimulates motility, thus counteracting the two main factors involved in the pathogenesis of the peptic ulcer and certainly of the gastric ulcer. 24 references.

000729 Campbell, Magda. New York University, Washington Square, New York, NY 10003 **Children's psychopharmacology unit.** Psychopharmacology Bulletin. 12(3):77, 1976.

The therapeutic effectiveness and safety of drugs is evaluated in autistic and other severely disturbed children. Levodopa produced improvement on the Clinical Global Impressions (CGI) measure in five of 12 schizophrenic children. Indices of improvement included decreased negativism, increased energy, motor initiation, and play in hypoactive children. Adverse effects of levodopa included vomiting, irritability, stereotypies, motor retardation and increased aggressiveness. Levoamphetamine produced improvement on the CGI in two of 11 children. Side-effects of levoamphetamine included exacerbation of preexisting stereotypies, emergence of new stereotypies and transient weight loss. There was no apparent correlation between blood serotonin levels and behavioral changes associated with either drug but a correlation between electroencephalogram (EEG) changes and clinical response was noted, especially with levodopa treatment. Within the patient group, low intellectual functioning was associated with high serotonin levels. In patients with florid psychosis, serotonin levels are generally higher than in patients who are in remission or partial remission. It is concluded that levodopa merits further study in autistic children because of its stimulating behavioral effects.

000730 Campbell, Magda. Department of Psychiatry, New York University Medical Center, New York, NY 10016 **Biological interventions in psychoses of childhood.** In: Schopler, E., Psychopathology and child development. New York, Plenum, 1976. 395 p. (p. 243-270).

Biological interventions in the treatment of childhood psychoses are reviewed, stressing that all physical therapies (psychosurgery, insulin and convulsive shock treatment) have largely been replaced by psychopharmacology. Relative prominence is given to major tranquilizers, (phenothiazines, butyrophenones, thioxanthenes, indoles) lithium and the hormones. Suitable information is also presented on hypnotics, anticonvulsants, sedatives, stimulants, antidepressants, minor tranquilizers, hallucinogens and L-dopa. No specific drug is most effective in reducing the various symptoms of individual children. Currently available compounds are most effective with insomnia, hyperactivity, impulsivity, irritability, disorganized behavior, psychotic thought disorder and certain types of aggressivity. The need for uniformity in classifying child psychoses is stressed in light of its potential value in predicting responses of children to specific drugs. The relatively new concept of orthomolecular treatment which suggests treatment of mental disease by providing the optimum molecular environment, especially the optimum concentration of substances normally present in the human body and brain, is also treated. 20 references.

000731 Dalske, H. Frederick; Wolf, Gerald L. Dept of Pharmacology, University of Nebraska College of Medicine, Lincoln, NE 68508 **Agents affecting adrenergic function in antihypertensive therapy -- II.** Nebraska Medical Journal. 61(7):227-230, 1976.

The effects of guanethidine and clonidine on adrenergic function in antihypertensive therapy are examined. The normal sequence of events during neurochemical transmission at the adrenergic neuron and the effect of guanethidine on adrenergic transmission are diagrammed. Clonidine does not block adrenergic receptors: its locus of action is thought to be the medullary vasomotor center, where its ability to stimulate central alpha-adrenergic receptors leads to inhibition of sympathetic outflow of the periphery. This diminution of sympathetic discharge is sufficient to suppress central pathways normally active in controlling blood pressure. Side-effects and dosage considerations of both drugs are discussed.

000732 Diehl, L. W.; Werner, W. Psychiatrische Klinik der Freien Universitat Berlin, Nussbaumallee 36, D-1 Berlin 36, Germany **/Serum levels, psychometric and psychopathological findings in complex epileptics on high-dosage therapy with carbamazepine (Tegretal)./** Befunde zur Psychopathologie, Psychometrie und Serumkonzentration unter hoch dosierter ambulanter Behandlung mit Carbamazepin (Tegretal) bei komplizierten Epilepsien. Bibliotheca Psychiatrica (Basel). No. 151:201-208, 1975.

A clinical test was made of the effectiveness of high, and very high dosage of carbamazepine long-term therapy in refractory epileptics and in patients with epilepsy complicated by mental illness. Seven complex epileptics were given 1200 to 1600mg/day or 1600 to 2400mg/day carbamazepine on an outpatient basis. Seizures were arrested in three patients and reduced in four. Psychopathological and psychometric findings showed positive improvement. Serum levels were optimal, if fractionally high. The risk in high dosage barbamazepine therapy is minimal if each patient's tolerance is carefully appraised. 11 references.

000733 Domzal, Teofan. Klinika Neurologiczna Centrum Ksztalcenia Podyplomowego WAM, ul. Szaserow 128, 00-909 Warzawa, Poland **/Trial of a new therapy of Huntington's chorea./** Proba nowego sposobu leczenia plasawicy Huntingtona. Neurologia i Neurochirurgia Polska (Warszawa). 10(1):45-48, 1976.

A new chemotherapeutic approach to Huntington's chorea is suggested, based on stimulation of the activity of the cholinergic system rather than on blocking of the dopaminergic system, as has been done in previous tests. A group of patients with Huntington's chorea, including five males and three females, 37-63 years of age, was treated with various acetylcholine precursors and cholinesterase blocking agents. Results showed significant improvement in four patients, moderate improvement in two, and slight improvement in two. Further research along this line of therapy is suggested. 8 references.

000734 Dowzenko, Anatol; Buksowicz, Czeslaw; Kuran, Wlodzimierz. Instytut Psychoneurologiczny, Sobieskiego 1/9, 02-957 Warszawa, Poland **/Effect of Coretal-Polfa (oxprenolol) on parkinsonian tremor and benign essential tremor./** Wplyw Coretalu-Polfa (oksprenolol) na drzenie parkinsonowskie i na drzenie samoistne. Neurologia i Neurochirurgia Polska (Warszawa). 10(1):49-53, 1976.

Coretal, a beta-adrenergic receptor blocking agent, was administered to 12 patients (eight females and four males, average age 58.5years) with Parkinson's syndrome with evident tremor, and to four patients with benign essential tremor in a single-blind trial. During the first 3 weeks the patients were adminstered 60-120mg Coretal daily. During the following 3 weeks they were given placebo. Improvements were observed in seven patients with Parkinson's syndrome and in three of the four cases of idiopathic tremor. Transient side-effects were observed in two cases. It is concluded that Coretal may be used beneficially in the treatment of parkinsonian tremor and benign essential tremor. 16 references. (Author abstract modified)

000735 Dringoli, R.; Guazzi, B.; Lanzoni, L. Istituzioni Riunite in Campansi, Reparti di Assistenza Geriatrica, Siena, Italy **/Clinical study of the effects of Vincamin in senile dementia syndrome./** Studio clinico controllato sugli effetti della vincamina nel decadimento mentale senile. Giornale di Gerontologia (Firenze). 23(12):1052-1062, 1975.

Following a short nosography of senile dementia syndrome and a brief review of latest achievements in the field of geriatric physiopathology, the results of long-term administration of Vincamin to a group of 32 hospitalized patients showing mental decay of vascular origin, as well as peripheral arteriosclerotic vascular symptoms are reported. The patients included 18 males and 14 females, aged 50 to 89, average age 72. After 60 and 120 days of Vincamin therapy a statistically significant improvement of subjective symptoms was observed, together with improvement of mental symptoms. Patients given placebo reported gradual worsening of symptoms. 20 references. (Author abstract modified)

000736 Duche, D.-J. Clinique de Psychiatrie Infantile, Hopital de la Salpetriere, 47, boulevard de l'Hopital, F-75634 Paris, France **/A double-blind study of the psychoanaleptic activity of the amineptic (1694) in retarded children without character disorders./** Etude a double insu de l'activite psychoanaleptique de l'amineptic (1694) chez les infants debiles non caracteriels. Revue de Neuropsychiatrie Infantile (Paris). 24(3):173-177, 1976.

The tolerance and therapeutic effect of the amineptic compound 1694 tested on 30 female retarded children aged 7 to 13 years is studied. Some of the children received placebos, others a dose of 50mg. of 1694 for 6 weeks. The double-blind crossover method was used to assure accuracy of the results. Notes were made on the children's behavior by a medical psychological/pedagogical team of experts. The results show a high tolerance with definite improvements in behavior in taking 1694.

000737 Faglioni, P.; Gasparini, M.; Spinnler, H. Centro di Neuropsicologia, Universita di Milano, Milan, Italy **/Outcome of Parkinsonism after 2 years of L-DOPA plus Ro4-4602./** Andamento della sindrome di Parkinson nel corso di terapia biennale con L-DOPA associata a Ro4-4602. Rivista di Patologia Nervosa e Mentale (Firenze). 96(4):270-286, 1975.

A study was made of 21 patients with Parkinson's disease who were treated with L-DOPA together with an extracerebral dopadecarboxylase inhibitor (Ro4-4602) and with triesyphenidyl. Over a period of 2 years seven assessments were made, along with a number of neurological and psychometric tests. At the beginning of the second year of treatment, the signs and symptoms of Parkinson's disease began to worsen, and increased disability was also manifested. The question of whether deterioration was the consequence of L-DOPA administration or whether it was simply the outcome of inadequacy of drug treatment during a period of natural worsening of the disease is discussed. Conclusion is that reduction in the therapeutic effect of the L-DOPA associated with Ro4-4602 occurs, and that this usually takes place at about the 10th to 13th month of therapy. 24 references.

000738 Flandin, F. Travail du Service d'Endocrinologie, CHU Purpan, F-31052 Toulouse, France **/The use of dipotassium chlorazepate at high dosage in treatment of obesity./** La place du clorazepate dipotassique a fort dosage dans les cures d'obesite. Revue de Medecine Psychosomatique (Toulouse). 18(2):205-209, 1976.

The use of dipotassium chlorazepate in the treatment of obesity is examined on the basis that anxiety or depression is often a cause of overeating. Fifty overweight women 14-62 years were restricted to a diet of 1,000-1,200 calories each day and given 150mg of either dipotassium chlorazepate or a placebo before each meal during a minimum hospitalization of 1 month. With the active product a 7-10kg decrease in weight

in 1 month was observed. The medication was perfectly tolerated although there were several cases of slight somnolence remedied by a decrease in dosage. With the placebo the results were less constant: loss of weight was slower, cheating on the diet was more frequent and the anxiety factor persisted. It is concluded that effective treatment of obesity should include psychological comprehension of the patient and a psychotherapeutic approach using a tranquilizer.

000739 Gajkowski, Kazimierz; Zalejski, Stanislaw. Klinika Neurologiczna Instytutu Ksztalcena Podyplomowego WAM, Szaserow 2, 04-293 Warszawa, Poland /**Comparative evaluation of seizure provocation methods with sleep deprivation and Brietal in epileptics.**/ Porownawcza ocena metod prowokacji pozbawieniem snu i Brietalem w padaczce. Neurologia i Neurochirurgia Polska (Warszawa). 10(2):267-272, 1976.

In a comparative evaluation of seizure in suspected epileptics, 19 patients in whom routine EEG investigations failed to show epileptiform, were subjected to sleep deprivation and intravenous administration of 1% Brietal solution. In cases in which sleep deprivation provoked pathological changes, Brietal gave a similar result but evoked focal changes more frequently. In some cases, in which sleep deprivation was ineffective, Brietal provoked slight changes. Both methods may be used for provocation, and Brietal may be more suitable in cases with suspected focal lesions. 14 references. (Author abstract modified)

000740 Gittelman-Klein, Rachel; Klein, Donald F. Child Development Clinic, Long Island Jewish-Hillside Medical Center, Hillside Division, Glen Oaks, NY 11004 **Methylphenidate effects in learning disabilities: psychometric changes.** Archives of General Psychiatry. 33(6):655-664, 1976.

The effect of methylphenidate therapy on the cognitive performance and academic achievement of children with learning deficits was investigated. Sixty one children, 7-13 years of age of average intelligence with appreciable learning lags, but no behavior disorders, received placebo or methylphenidate hydrochloride for a 12 week period. Methylphenidate was instrumental in improving performance on many psychological tests, but did not affect performance on standardized achievement tests. None of the patient characteristics investigated was strongly predictive of drug effect. Methylphenidate seems to have a specific effect in visuomotor processes, which in turn positively affect performance tasks, but not verbal tasks. Under the conditions of this study, methylphenidate treatment alone is not useful for producing the amelioration of reading performance, although evidence for stimulant effects on children's cognitive functions is provided. 10 references. (Author abstract modified)

000741 Guilleminault, C.; Raynal, D.; Takahashi, S.; Carskadon, M.; Dement, W. Sleep Disorders Clinic and Laboratory, Stanford University School of Medicine, Stanford, CA 94305 **Evaluation of short-term and long-term treatment of the narcolepsy syndrome with clomipramine hydrochloride.** Acta Neurologica Scandinavica (Kobenhavn). 54(1):71-87, 1976.

Clinical examinations, questionnaires and 24 hour or 36 hour polygraphic recordings were performed on 21 adult patients with the narcolepsy syndrome to investigate the short-term and long-term effects of clomipramine hydrochloride. Cataplexy was improved by the medication, but tolerance was observed after 4 1/2 months of treatment. Clomipramine hydrochloride induced significant changes in the sleep electroencephalograph, chin electromyograph and electrooculography. In two patients, clomipramine hydrochloride caused a nocturnal myoclonia that produced insomnia. Sexual side-effects were seen with clomipramine hydrochloride, particularly in males. A combination of clomipramine hydrochloride and levodopa apparently prevented this difficulty in one patient. A rebound of cataplexy was seen during the 15 days following withdrawal of the drug. Methysergide maleate was found to be ineffective on cataplexy in four patients. 23 references. (Author abstract)

000742 Hague, William H.; Wilson, Lawrence G.; Dudley, Donald L.; Cannon, Dale S. Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA 98195 **Post-detoxification drug treatment of anxiety and depression in alcohol addicts.** Journal of Nervous and Mental Disease. 162(5):354-359, 1976.

A study was undertaken to assess the effectiveness of treating alcoholics after detoxification for the very commonly observed syndrome of anxiety, depression and somatic complaints. Forty five comparably addicted male alcoholics with anxiety or mixed anxiety depression from an inpatient alcohol treatment ward comprised the treatment group. Twenty three patients received thioridazine treatment, and 22 received placebo treatment in a double-blind fashion after acute withdrawal from alcohol. Progress over a 4 week period was measured with standard rating instruments. Both placebo and active medication groups improved symptomatically during the 4 week program. The thioridazine group had significantly better improvement in sleep disturbance than the placebo group. There was also significantly better improvement in anxiety with thioridazine as compared with placebo. The placebo group had significantly better work and activity than the thioridazine group, and it was felt that active drug effect might actually hamper some patients in their rehabilitative effort, especially if phenothiazine of the more sedating variety are used. Since alcohol rehabilitation generally utilizes a wide range of activities, alertness and performance ability appear to be important factors in the rehabilitation program. It was concluded that although thioridazine treatment for some patients with anxiety and insomnia would appear to be quite helpful, its blanket use for the postdetoxification anxiety depression of the alcoholic might be detrimental for others and cannot be recommended as a routine treatment strategy in an alcohol rehabilitation program. 15 references. (Author abstract modified)

000743 Hardjawana, B.; Setyonegoro, R. Kusumanto; Budhiman, M.; Sobari, T.; Dhoemadi, E. Jakarta, Indonesia **Treatment of children with difficulties in learning with pyrithioxine (Encephabol) in Jakarta, Indonesia.** Report, Second Asian Conference on Mental Retardation. Tokyo, Japan League for the Mentally Retarded, 1975. (p. 84).

In a study aimed at reducing school failures and dropouts in Jakarta, Indonesia, pyrithioxine (Encephabol) was administered to 82 children, aged 8 to 12 with IQ 65 to 110, who showed learning difficulty, in an attempt to improve scholastic performance. Wechsler Intelligence Test for Children scores recorded before and after clinical trial were compared and correlated with evaluations by teachers, psychologists, and psychiatrists. Positive improvement in learning was demonstrated in 55.4% of the subjects, 21.4% showed no consistent improvement, and 23.2% showed no improvement. The medication was well tolerated. Difficulties were encountered in accurate differentiation of clinical and subjective data.

000744 Hsu, M. S.; Chen, A.; Lau, A.; Lee, S. C. Acupuncture Research Committee, Tri-Service General Hospital,

Taipei, Taiwan **Electroacupuncture and heroin addiction, a case report.** Chinese Medical Journal (Taipei). 22(3):214-217, 1975.

The case of a 26-year-old Briton who had been addicted to heroin for three years is discussed. The patient has been treated previously with methadone maintenance and psychotherapy without success. Treatment by acupuncture with electrical stimulation was undertaken. After ten treatments the heroin withdrawal syndrome was relieved and was much less severe than that experienced before. There were no complications. It is concluded that acupuncture might be better than psychotherapy or methadone maintenance in the management of narcotic withdrawal. 6 references.

000745 Ikeda, Teruaki; Morita, Shonosuke; Kobayashi, Yoshiyasu; Yamauchi, Toshio; Saito, Yoshiro; Fujieda, Toshiyoshi; Suwa, Nozomu. Otaru Second Metropolitan Hospital, Japan **On applying the combined therapeutic effects of the anti-Parkinson's disease drugs L-DOPA and Dopa decarboxylase inhibitor.** Psychiatria et Neurologia Japonica (Tokyo). 77(10):745, 1975.

The results of combined administration of L-Dopa and Dopa decarboxylase inhibitor anti-Parkinson disease drugs are compared with the results of administering L-Dopa alone. It was found that with combined administration, as compared with only L-Dopa administration, effect took hold earlier, improvement was sometimes more marked, side-effects were fewer, and that the amount of L-Dopa administered could be conserved from 20-25%. Symptoms of depression and insomnia were also reduced. It is concluded that there are definite advantages to using L-Dopa in combination with Dopa, but that the smallest possible dose should be used.

000746 Izumi, Teiji. Department of Psychiatry, Niigata University School of Medicine and Kodo Mental Hospital, Japan **Clinical studies with pindolol (Carvisken), a beta-adrenergic blocking agent, in the treatment of sinus tachycardia associated with the use of psychotropic drugs -- a double-blind study.** Clinical Psychiatry (Tokyo). 17(6):631-642, 1975.

Pindolol (carvisken), a beta interceptor, was tested with an inactive placebo in a double-blind study to test its effects on the sinus tachycardia associated with the use of psychotropic drugs. Group A contained 27 patients and group B contained 26 -- both groups suffered sinus tachycardia (above 90 pulse) from taking major tranquilizers. Administration was on a fixed thrice daily schedule with 5mg of pindolol in each tablet. Group A was given carvisken for 2 weeks, then the placebo for 1, then back to the carvisken; while Group B was given the placebo for 2 weeks, the carvisken for 1, then back to the placebo for 2 weeks. Pulse rate was reduced by 9.3-17 beats while taking carvisken and was within normal limits. Maximum results were obtained within 25 hours of administration. No prominent side-effects were noted. It is concluded that pindolol was very effective in controlling sinus tachycardia. 48 references.

000747 Kaiser, H. no address **/Disturbed sleep./** Der gestorte Schlaf. Koln, Deutscher Arzte, 1975. 216 p. DM14.

A handbook on the diagnosis and treatment of sleep disorders is presented. Analytic procedures are described, and results are related to therapeutic options. The pharmacology of sleep-inducing drugs, their clinical application, and their mechanism of action are discussed.

000748 Kales, Anthony; Kales, Joyce D.; Bixler, Edward O.; Scharf, Martin B.; Russek, Edward. Pennsylvania State University, Milton S. Hershey Medical Center, Hershey, PA 17033 **Hypnotic efficacy of triazolam: sleep laboratory evaluation of intermediate-term effectiveness.** Journal of Clinical Pharmacology. 16(8-9)399-406, 1976.

The hypnotic effectiveness of triazolam was evaluated in seven insomniac subjects with a standard protocol which included a 2 week consecutive period of drug administration. With short-term drug use, both sleep induction and sleep maintenance improved, with total wake time decreasing markedly. Following drug withdrawal, sleep difficulty significantly increased above baseline levels. The percent of rapid eye movement (QEM) sleep decreased significantly during both short and intermediate drug conditions. Following drug withdrawal, the percent of REM sleep was similar to baseline. Slow wave sleep was significantly decreased for both drug conditions, and following withdrawal, it returned completely to the baseline level. The data indicate that triazolam is effective for short-term use, loses most of its effectiveness with intermediate term use, and its withdrawal is followed by a significant worsening of sleep. These findings are discussed in relation to potential labeling and promotion. Further research is needed on the amnesia associated with triazolam administration. 14 references.

000749 Kato, Hiroaki; Endo, Masako; Endo, Hideo; Kato, Ikuko. Noboribetsu E-Ai Hospital, Japan **The use of the beta-interceptor phendoral within the field of psychiatry.** Psychiatria et Neurologia Japonica (Tokyo). 77(10):745, 1975.

Phendoral, a beta-interceptor, was administered to 14 mental patients who complained of side-effects from other drugs they were taking. Specific side-effects were frequent pulse, chest pains, and tremors. It relieved side-effects very effectively in six cases, effectively in five, and had no effect in three cases. Rapid pulse was relieved in 12 of the 14, and chest sensations relieved in six of eight cases. Tremors were relieved in 10 of 13 of the patients. New side-effects such as dry mouth, sleepiness and insomnia appeared in 7 of the 14 patients. It was deemed effective in relieving the side-effects of other drugs.

000750 Kohler, C.; Kamoun, A.; Gailly, M.-T. Pavillon Jean Dechaume, Hopital Sainte-Eugenie, F-69230 St Genis Laval, France **/Molecule 1694 in the treatment of children with cerebral motor disorders or developmental psychomotor disorders./** Interet du 1694 chez les enfants infirmes moteurs cerebraux, ou presentant un trouble de developpement psychomoteur. Revue de Neuropsychiatrie Infantile (Paris). 24(1-2):57-60, 1976.

The use of the molecule 1694 in the treatment of children with cerebral motor disorders or developmental psychomotor disorders is discussed. Results indicate that a dosage of 50mg/daily and 100mg/daily of 1694 is effective and well tolerated. 1694 favors group integration of the children and decreases anxiety, inertia, apathy and inhibition. Improved cooperation in reeducation classes is observed which in turn increases the child's verbal and motor progress.

000751 Kolasa, Maria; Reichowa, Janina; Bieniowa, Anna. Klinika Neurologiczna, ul. Botaniczna 3, 30-503 Krakow, Poland **/Results of L-dopa treatment in Parkinsonism./** Wyniki leczenia Parkinsonizmu L-Dopa. Przeglad Lekarski (Warszawa). 33(3):407-410, 1976.

The results of treatment of 37 cases of Parkinsonism with L-dopa are presented. The patients, 40-78 years old with duration of illness of 6 months to 28 years, were given 3-4mg daily for an average of 19 months. Results were very good in 29% of

the cases, good in 55% and slight improvement was observed in 8%. Severe symptoms of low tolerance were observed in 8% and treatment was discontinued. The drug reduced hyperkinesis in 81%, reduced muscular rigidity in 70% and decreased tremor in 51% of the cases. Improvement was observed to depend on the duration of the illness and the patient's age. 9 references. (Author abstract modified)

000752 Krasner, N.; Moore, M. R.; Goldberg, A.; Booth, J. C. D.; Frame, A. H.; McLaren, A. D. Department of Materia Medica, Stobhill General Hospital, Glasgow G21 3UW, Scotland **A trial of fenfluramine in the treatment of the chronic alcoholic patient.** British Journal of Psychiatry (London). 128:346-353, 1976.

In a double-blind trial, 50 male chronic alcoholic patients were treated with either fenfluramine in a dose of 60mg or 120mg daily, or with identically prepared placebo tablets. Patients were interviewed on admission to the trial and then at 4 weekly intervals for a period of 1 year, and blood levels of delta-aminolaevulinic acid dehydratase and gamma-glutamyl transpeptidase and fenfluramine were determined. The efficacy of fenfluramine at the two dose levels was compared with placebo on the basis of the number of lapses indicated by the clinical history and also by alterations in the biochemical indices. Twenty seven patients completed the period of observation, there being nine in each of the three groups. Those receiving 120mg fenfluramine daily showed significantly fewer lapses than either of the other two groups on biochemical but not on clinical criteria. Overall assessment revealed that three of the nine patients receiving the high dose of fenfluramine had a good result during the period of the trial, but there were none in the 60mg group or in those receiving placebo. More extensive trials of fenfluramine in the treatment of chronic alcoholism are indicated. 41 references. (Author abstract)

000753 Kudo, Yoshio; Kawamura, Kunitaka; Konishi, Terou; Minami, Katsumasa; Saito, Masaki; Tsukamoto, Muneyuki; Tsutsumi, Shigetoshi; Yura, Ryozo. Osaka Police Hospital, Osaka, Japan **Double-blind comparative test of Lorazepam for psychoneurosis.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(5):563-576, 1975.

The effect of lorazepam on various kinds of neurosis was compared via the double-blind test with the effect of the standard drug, diazepam, in a total of 134 neurotic patients, half of whom were treated with lorazepam and half with diazepam. Doctors could not find significant differences between the two drugs regarding the general rate of improvement among the patients, differences in degree of illness with change in treatment, nor differences in severity of the neurosis among the two groups. Five percent of the patients thought that diazepam made them significantly better than lorazepam, while 1% of depressed neurotics found lorazepam better. No differences could be found in the rate of side-effect appearance in either of the two groups. 13 references.

000754 Kuran, Wlodzimierz. Instytut Psychoneurologiczny, Sobieskiego 1/9, 02-957 Warszawa, Poland **/Modern views on the pathophysiological substrate of involuntary movements in Huntington's chorea./** Wspolczesne poglady na patofizjologiczne podloze ruchow mimowolnych w plasawicy Huntingtona. Neurologia i Neurochirurgia Polska (Warszawa). 10(1):75-80, 1976.

The research on certain biochemical and clinical aspects of Huntington's chorea (HC) is reviewed. Unlike Parkinson's syndrome, in HC the dopamine content of the CNS is undisturbed. However, some studies have found that treatment with phenotiazines or butyrophenone reduces blocking of dopaminergic receptors in the CNS. It is believed by some that HC is caused by hyperactivity of these receptors. Administration of cholinesterase blocking agents has also been found to reduce involuntary movements. Such movements are often accompanied by a low level of glutaminic acid decarboxylase (GAD) in the CNS, which has led some researchers to believe that GAD deficiency is responsible for involuntary movements. The need for further research is suggested. 30 references.

000755 Linnoila, M.; Viukari, M. Box 2921, Duke University Medical Center, Durham, NC 27710 **Efficacy and side effects of nitrazepam and thioridazine as sleeping aids in psychogeriatric in-patients.** British Journal of Psychiatry (London). 128:566-569, 1976.

The efficacy and side-effects of 10mg of nitrazepam and 25mg of thioridazine as sleeping aids were measured in 20 psychogeriatric inpatients during the 14th night and morning of drug administration. The trial used a double-blind, crossover design. The effect of nitrazepam was slightly faster than that of thioridazine. After thioridazine, but not after nitrazepam, the patients slept significantly longer than after placebo. Nitrazepam, but not thioridazine, significantly impaired patients' abilities to move and to conduct everyday activities. It is concluded that thioridazine is a suitable sleeping aid for psychogeriatric patients, but that nitrazepam should be avoided. 14 references. (Author abstract)

000756 Lorenzini, R.; Marega, M. G. Villa di Salute Trofarello, Torino, Italy **/Clinical experiences with the combined use of two neuroleptics, clothiapine and haloperidol, in the treatment of certain mental diseases./** Nostre esperienze cliniche con l'associazione di due neurolettici: clotiapina + aloperidolo nel trattamento di alcune malattie mentali. Rassegna di Studi Psichiatrici (Siena). 65(4):751-757, 1976.

A clinical trial was made of the combined administration of two neuroleptics, clothiapine and haloperidol, to 75 patients with manic excitation state, schizophrenia, states of confusion, paranoia, and excitement of senile psychosis. Results proved satisfactory in the majority of cases, as these two drugs are effective sedatives. The problem of determination of dosage was successfully resolved. 19 references.

000757 Luzi, T.; Bocci, U.; Consoloni, E.; Tolone, S. F.; Palaia, R. Ospedale Psichiatrico di Castiglione delle Stiviere, Mantua, Italy **/Disordered behavior of epileptics and current therapeutic orientations./** Le turbe della condotta negli epilettici e gli attuali orientamenti terapeutici. Rassegna di Studi Psichiatrici (Siena). 65(2):249-303, 1976.

Present means of controlling behavior of epileptics are reviewed. Emphasis is placed on chemotherapy. Although limited in terms of controlling undesirable side-effects, psychopharmacology, with benzodiazepine in particular, provides increasingly effective therapeutic means in working with epileptics. A study and definition of personality is undertaken. It is suggested that the relationship between the evolution of epilepsy and neurotic tensions within the family environment be further investigated. 95 references.

000758 Maltaverne, S.; Jonnard, D.; Broussolle, P. Hopital du Vinatier, Lyon, France **/A clinical trial of Pervincamine Forte Retard in neuropsychiatry./** Essai Clinique de pervincamine forte retard en neuro-pschiatrie. Revue de Neuropsychiatrie de L'Ouest (Rennes). 12(49):33-43, 1975.

A study of 52 elderly patients taking Pervincamine Forte Retard to alleviate cerebral vascular insufficiency is presented. The median age of the subjects was 73 years, and 49 of the 52 subjects were neuropsychiatric patients. No abnormal side-effects were noted. Psychometric tests were administered before, during and after the treatment. In 73% of the cases psychointellectual symptoms of those suffering from insufficient cerebral circulation improved and intellectual functions such as visual recall improved. Pervincamine Forte Retard also decreases depressive behavior tendencies in the elderly, as determined by the Honigfeld and Klett Nurses Observation Scale.

000759 Mangoni, Alfonso. Department of Psychiatry, Medical School, University of Cagliari, Cagliari, Sardinia, Italy **Psychopharmacology of the peptic ulcer.** Medicina Psicosomatica (Roma). 20(1):11-17, 1975.

Principal data to bear in mind in choosing the best drug for treatment of the peptic ulcer are outlined. Clinical, psychodynamic and biological criteria were the bases for choosing these drugs. The clinical and psychodynamic considerations took into account the personality of the patient, his conflicts, dynamic reactivity and defense mechanisms. Biological factors such as characteristics of vagus stimulation, gastrin, and neuroendocrine stimuli were also considered. Caution is recommended in the administration of some psychotropic drugs such as reserpine, which causes worsening of the ulcer condition. Certain antidepressant drugs exacerbate ulcerous conditions, as well. It is concluded that the most appropriate psychopharmacological therapy for the ulcer patient involves anxiety reducing drugs, such as benzodiazepines or an antidepressant such as monoaminoxidase inhibitors. In some cases a combination of the two drugs is recommended. It is suggested that much remains to be done in this field, especially regarding the mechanism of action of drugs at the metabolic level. 11 references.

000760 Marchesi, G. F.; Quattrini, A.; Scarpino, O.; Dellantonio, R. Clinica delle Malattie Nervose e Mentali e Insegnamento di Psicologia dell'Universita di Ancona, Ancona, Italy **/Therapeutic effects of taurine in epilepsy: a clinical and polyphysiographic study./** Effetti terapeutici della taurina nella epilessia. Indagine clinica e polifisiografica. Rivista di Patologia Nervosa e Mentale (Firenze). 96(3):166-184, 1975.

Effect of taurine on 37 epileptic patients in whom frequency and duration of seizures was considerable, is reported. Of these patients, 15 had temporal lobe epilepsy, 10 had Lennox-Gastaut syndrome, 5 had generalized epilepsy (either convulsive or nonconvulsive), and 3 brothers had myoclonic familial progressive epilepsy. All groups reported similar results and improvement was noted in about 50% of the cases both physically and psychologically. Psychological improvement was mostly related to attention and memory. No pathological aspect of personality appeared to be modified. 44 references.

000761 McClane, T. K.; Martin, W. R. Watson Clinic, Lakeland, FL **Subjective and physiologic effects of morphine, pentobarbital, and meprobamate.** Clinical Pharmacology and Therapeutics. 20(2):192-198, 1976.

The development and validation of methods for the pharmacologic characterization of psychoactive drugs as well as methods for identification of their reinforcing properties are discussed. The effects of pentobarbital and meprobamate on postrotational nystagmus were studied using electro-oculography. Frequency was found to be a more precise and less variable measure of postrotational nystagmus than duration. Under control conditions frequency and duration were correlated. They were not correlated so closely when drugs were administered. This finding suggests that the measures of frequency and duration are differentially effected by pentobarbital and meprobamate. It is suggested that the difference might be a manifestation of different physiologic processes and, therefore, their concomitant measurement might allow the identification of the selective effects of depressants. It was also concluded that meprobamate is 1/15 to 1/20 as potent as pentobarbital in inducing sedation and enhancing postrotational nystagmus. 6 references.

000762 Miyakoshi, Takashi. Department of Psychiatry, Tohoku University, Sendai, Japan **Comparison of bromazepam (RO5-3350), a new tranquilizer for psychosis with diazepam by a double-blind crossover examination in the treatment of neurosis.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(7):833-846, 1975.

The new tranquilizer, bromazepam (RO-3350) and diazepam were tested and their relative effectiveness compared. Bromazepam was tried on 38 neurotic, depressed, and schizophrenic patients with an effectiveness of 13% with no specific side-effects. Then diazepam was compared to bromazepam via the double-blind test with outpatient neurotics. Thirty seven of these patients were given 5mg capsules of either bromazepam or diazepam for a period of 4 weeks, then the medicines were switched. Results indicated that no significant differences in the effects of the two drugs could be found. Both also produced side-effects of weakness, insomnia, dizziness, or loss of appetite. 22 references.

000763 Morcaldi, L.; Camardese, M.; Palumbo, E. Ospedale Neuropsichiatrico Don Uva, Potenza, Italy. **/Use of Leponex in the treatment of chronic psychiatric problems: clinical study./** Il Leponex nel trattamento di alcuni quadri psichiatrici cronici: studio clinico. Rassegna di Studi Psichiatrici (Siena). 65(4):771-782, 1976.

The drug Leponex was administered to 31 psychopathic, schizophrenic, and oligophrenic patients, male and female, ranging in age from 23 to 62, to test its effectiveness. The drug was administered orally. Leponex was found to be more effective among young patients, with no distinction between males and females. To its overall effectiveness in normalizing behavior, it must be added that Leponex generated no side-effects. 1 reference.

000764 Nielsen, N. P.; Drago, F. C. Ospedale Psichiatrico Provinciale di Como, Como, Italy **/Use of dibenzepine retard in the treatment of alcoholic depression./** L'impiego della dibenzepina "retard" nel trattamento delle depressioni alcooliche. Rassegna di Studi Psichiatrici (Siena). 65(4):735-750, 1976.

A dibenzepine preparation with retard action was tested in 25 alcoholic patients with symptoms of depression. The results, confirmed by the Hamilton and Zung rating scales, suggest positive thymoanaleptic action of the drug; the retard action affords daily doses that are free from any form of dependence on the part of the patient. 62 references.

000765 Nishizono, Masahisa. Department of Psychiatry, Fukuoka University School of Medicine, Fukuoka, Japan **Psychodynamics of psychotropic drug therapy.** Clinical Psychiatry (Tokyo). 17(11):1132-1147, 1975.

The theoretical considerations are discussed of drug effects in various types of mental illness. Reasons for variation in ef-

fects from one person to another are emphasized, and it is noted that placebo reactions, the therapeutic environment, the patient's personality, and the therapist's personality are all important in determining the effectiveness of drug therapy. Specific discussions follow on drug therapy in relation to neurosis, neurotic loss of appetite, depression, and schizophrenia. Statistics as well as a recap of the research of others is provided to give a general idea of results that can be expected from various drug therapies such as phenothiazine, butyrophenone, piperdine, butyrophenone, and thioxanthene. 36 references.

000766 Niskanen, Pekka; Viukari, Matti. Psykiatriska Kliniken, Lappviksvagen, SF-00180 Helsingfors 18, Finland **/Effects of dikalium clorazepate on serum levels and metabolites./** Resorption och omvandling av dikaliumklorazepat till nordiazepam. 29(5):387-392, 1975. Nordisk Psykiatrisk Tidsskrift (Kungsbacka).

A clinical evaluation of a new benzodiazepine derivative, chlorazepate, was made. The serum levels and/or their metabolites were analyzed. Simultaneously, Tranxilen and its Finnish equivalent YT-11 were compared in a single blind crossover study. A single dose 10mg or 20mg of dikalium chlorazepate was given to 13 alcoholic patients, all men under 50 years old. The serum levels were analyzed by electron capture gas chromatography after 1, 2, 4, and 6 hours. The analysis showed only nordiazepam (N-demethyldiazepam) in the serum samples. Great individual variations were seen in the serum level of 100% for the same patient and drug, from 1 week to another. No significant secondary effects were noted. The differences of the mean levels between Tranxilen and YT-11 are not statistically significant. 7 references.

000767 Ohmoto, Takashi; Kishikawa, Hidemi. Department of Neurosurgery, Okayama University, Japan **L-Dopa therapy combined with peripheral decarboxylase inhibitor (MK-486) in Parkinsonism.** Psychiatria et Neurologia Japonica (Tokyo). 77(7):537, 1975.

The combined effect on Parkinson's disease of L-Dopa (with its decarboxylase inhibitor effect on the peripheral brain area) and MK-486 (L-alpha-hydrazinomethyldopa) was debated then tested. Tests on cats showed that with 100mg and 10mg per kilogram of body weight of L-Dopa and MK-486 respectively, dopa and dopamine within the blood and brain increased three to four times. Eighteen Parkinson patients were given L-Dopa and MK-486 in a ten to one dosage ratio. In ten patients (67%) this treatment was effective against akinesia. The effect on tremors was not as marked. Dyskinesia was noted as a prominent side-effect.

000768 Ost, Lars-Goran; Gotestam, K. Gunnar. Psychiatric Research Center, University of Uppsala, Ulleraker Hospital, S-750 17 Uppsala, Sweden **Behavioral and pharmacological treatments for obesity: an experimental comparison.** Addictive Behaviors. 1(4):331-338, 1976.

A comparison is reported of the effectiveness of behavior therapy, pharmacological treatment (fenfluramine), and a waiting list control condition in the treatment of obesity. Forty five subjects at least 15% overweight were randomly assigned to three groups of 15 each. Subjects were weighed before and after treatment and 12 months following treatment. Results showed that all subjects reduced their initial weight significantly but regained most of their loss during the year after treatment. Comparisons between groups indicated that the behavioral treatment was more effective than the pharmacological in reducing the subjects' weight. 17 references. (Author abstract modified)

000769 Perzynski, Janusz. Klinika Psychiatryczna Instytute Chorob Ukladu Nerwowego AM, ul. Abramowicka 2, 20-442 Lublin, Poland **/Paranoid psychosis with oneiroidal elements during the course of Redlich-Flatau's disease./** Psychoza urojeniowa z elementami oneiroidalnymi w przebiegu choroby Redlicha-Flataua. Psychiatria Polska (Warszawa). 9(1):77-80, 1975.

The case of a 22-year-old woman with Redlich-Flatau's disease is described. At first, only mild neurotic symptoms were observed: loss of concentration and memory, insomnia, indecision, and anxiety. Two weeks before hospitalization the patient suffered severe oneiroidal experiences relating to rape and prostitution. Psychotic tendencies subsequently appeared: fear, lowered drive, paranoia, and depression. Following administration of relanium and haloperidol, the patient was discharged. 14 references.

000770 Peta, G.; Ravenna, M.; Borghi, G.; Battacchi, M. W.; Cavazzuti, F. no address **/Action of Trazodone on mental functions of the aged./** Azione del Trazodone sulle funzioni mentali dell'anziano. Medicina Psicosomatica (Roma). 20(4):415, 1975.

The influence of Trazodone on mental functions of the aged was examined at the Third Congress of the International College of Psychosomatic Medicine (Rome, September 1975). An experimental study of the effect of Trazodone on the aged was described. The cognitive component was separated from the emotional component to see which one was more affected by the drug. Two tests were used: 1) transfer of discrimination learning where the emotional component is minimal, and another in which emotion is highly significant and interferes in the execution of the test. Two groups were used, one experimental and the other a control group treated with a placebo. Results were discussed at the Congress.

000771 Porot, M. J.; Perol, Y.; Coudert, J. no address **/Bromazepam in psychosomatic medicine./** Le bromazepam en medecine psychosomatique. Medicina Psicosomatica (Roma). 20(4):420, 1975.

Use of bromazepam in treating psychosomatic disorders was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September 1975). Bromazepam was given to 200 patients suffering from sleep disorders, physical anxiety manifested in the cardiovascular and respiratory systems, and mental anxiety. Results showed that 77% of the cases yielded good results, and tolerance was excellent in all cases. In addition, results are better than those obtained with other benzodiazepines in at least 68% of the cases.

000772 Prien, Robert F.; Klett, C. James; Caffey, Eugene M., Jr. Psychopharmacology Research Branch, NIMH, Bethesda, MD **Polypharmacy in the psychiatric treatment of elderly hospitalized patients: a survey of 12 Veterans Administration hospitals.** Diseases of the Nervous System. 37(6):333-336, 1976.

In a survey of 12 Veterans Administration hospitals, the use of drug combinations (polypharmacy) in the psychiatric treatment of elderly hospitalized patients is examined. Numerous articles in the professional and lay literature allude to "overmedication" of institutionalized elderly patients, but these are based mainly on anecdotal data. Most surveys of polypharmacy have been conducted with primarily nongeriatric schizophrenic populations. These surveys report multiple drug use in 24% to 41% of the patients. The only survey to evaluate a predominantly geriatric population is a single hospital study, which indicates that patients over the age of 70 are less likely

to receive antipsychotic drug combinations than their younger counterparts. There is need for systematic surveys of polypharmacy in treatment of the elderly. Without information on the treatments actually administered to elderly patients, it is difficult to evaluate the appropriateness of combined medications or even identify combinations requiring study. 13 references. (Author abstract modified)

000773 Robert, Giovanni; Rocco, Gianluigi. Universita degli Studi di Genova, Istituto di Psichiatria, Genova, Italy **/Agonists and antagonists in the treatment of drug addiction./** Agonisti ed antagonisti nel trattamento delle tossicomanie da narcotici. Rivista di Psichiatria (Roma). 10(3): 250-267, 1975.

Overview suggests that utilization of drug substitutes to cure the drug addict was neither beneficial to the patient nor acceptable as a panacea for his complete cure. Disagreement as to the real value of drug substitution in both past and present medical practice was indicated. Conclusion was that the use of methadone (10 to 20 mg/day), naloxone (200 to 500 mg/day), and maltrexone (50 mg/day) used as substitute drugs were considered acceptable but by no means a complete cure for the addict. Ample description of the characteristics of these drugs was given. 49 references.

000774 Rutkowski, Ryszard. Klinika Psychiatryczna PAM, ul. Broniewskiego 1/32, 71-460 Szczecin, Poland **/Note on the dynamics of the psychoorganic process./** Przyczynek do zagadnienia dynamiki procesu psychoorganicznego. Psychiatria Polska (Warszawa). 9(1):81-84, 1975.

The case of a 22-year-old male with a psychoorganic syndrome is described. Early diagnosis was schizophrenia with apathetic symptoms and other minor complaints of headaches, restlessness, moodiness, etc. The patient was treated with neuroleptic drugs, but reported that his headaches increased after taking the drug. Subsequent pneumoencephalography revealed minor symmetrical hydrocephaly with slight cortical atrophy. Apathetic psychoorganic syndrome was diagnosed. Treatment with bimanol has resulted in considerable improvement. 14 references.

000775 Schmitz, I.; Janzik, H. H.; Mayer, K. Neurologische Klinik der Universitat Tubingen, Liebermeisterstrasse 18-20, D-74 Tubingen, Germany **/Personality structure and sexual behavior of epileptics under long-term treatment with DPH./** Personlichkeitsstruktur und Sexualverhalten Anfallskranker unter Langzeitbehandlung mit DPH. Bibliotheca Psychiatrica (Basel). No. 151:176-181, 1975.

The personalities and sexual attitudes of 19 male patients between the ages of 18 and 56 with temporal lobe epilepsy and receiving DPH (diphenylhydantoin) were evaluated to determine the cause of decreased sexual drive and impaired sexual potency often noted by this type of patient. DPH dosage was etween 200 and 300mg/day and was taken for an average of 3 years. Changes in sexual behavior occurred predominantly in the first 2 years after the beginning of treatment, after which the condition gradually improved. Findings indicated no link between epilepsy or DPH and impaired sexual behavior. A connection may exist between personality type and reaction to the disease, but the sampling here is too small for significance. DPH seems to increase the level of hypophyseal gonadotropic hormone, but a connection between this increase and sexual behavior is improbable.

000776 Schooler, Nina R.; Levine, J. Psychopharmacology Research Branch, NIMH, 5600 Fishers Lane, Rockville, MD 20852 **The initiation of long-term pharmacotherapy in schizophrenia: dosage and side effect comparisons between oral and depot fluphenazine.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(4):159-169, 1976.

Oral fluphenazine hydrochloride and depot fluphenazine deconate are compared for dosage equivalence and incidence of side effects during the early weeks of drug therapy. Schizophrenic patients were given either the drugs or placebo tablets or injections in a double-blind study. Results indicated that dosage equivalence may be set within the range of 5-60mg per day orally and 12.5-100mg every 3 weeks by depot injection. Symptoms involving the extrapyramidal system and sleep disturbance were observed in more than 20% of the patients. The results indicated no difference in incidence of side-effects. 3 references.

000777 Schott, G. Nervenklinik des Bereich Medizin, Humboldt Univ., Schumannstr. 20/21, DDR-1040 Berlin, Germany **/Acute and chronic psychiatric diseases of old age, their diagnosis and treatment./** Akute und chronische psychiatrische Krankheitsbilder des hoheren Lebensalters, ihre Diagnostik und Therapie. Zeitschrift fur Alternsforschung (Berlin). 30(4):305-311, 1975.

An overview of geriatric psychopathological symptomology, both acute and chronic, is given along with therapeutic recommendations. The special character that anxieties, sensory illusions, and hallucinations acquire when linked to the aging processes is probed, especially with regard to etiological factors. The confused mental states observed in many patients reflecting various states of consciousness, incoherent thinking and disorientation are also examined in reference to specific physiological and psychological etiologies from myocardial infarct to acute decompensation of a psychological nature. Pharmacotherapy of many of the aforementioned problems requires careful consideration of side-effects that may be precipitated in an aging patient; medications of choice are anxiolytic and antidepressants that contribute to regulation of the sleep/waking cycle. Combinations of the thioridazine group have been found to be especially effective in the treatment of personality disorders. A psychotherapeutic milieu including individual and group therapies should accompany psychopharmaceutical treatment, with special emphasis on achieving a secure, familiar environment. The treatment of a symptomatic psychosis of unclear etiology is discussed, as well as antihypertonic therapy of confused mental states resulting from circulatory disturbances. Drug therapies and/or psychotherapy indicated for delirium excitation, semiconsciousness, paranoid hallucinatory syndrome, and deteriorating conditions precipitated by stroke or other conditions are also outlined.

000778 Sellers, E. M.; Cooper, S. D.; Zilm, D. H.; Shanks, C. Clinical Pharmacology Program Addiction Research Foundation, 33 Russel St., Toronto, Ontario M5S 2S1, Canada **Lithium treatment during alcoholic withdrawal.** Clinical Pharmacology and Therapeutics. 20(2):199-206, 1976.

The efficacy of lithium carbonate was studied in 18 chronic alcoholic male patients in withdrawal. In mild alcoholic withdrawal, oral lithium carbonate, 0.3gm every 8 hr, diminishes subjective symptoms of withdrawal and normalizes performance on a motor tracking task. Patients who start lithium while drinking ethanol improve most probably because it takes longer than 3 days for lithium concentrations in the blood to plateau. Lithium does not importantly alter patterns of catecholamine excretion, blood pressures, heartrate, serum cyclic adenosine monophosphate (AMP), serum dopamine beta-hydroxylase (DBH), sleep pattern, or tremor amplitude during withdrawal. 34 references. (Author abtract)

000779 Suzuki, Shigemichi. Shizuoko Prefectural Hospital, Japan **Experiences with the long-term use of anatensol depot.** Psychiatria et Neurologia Japonica (Tokyo). 77(7):536, 1975.

Problems concerning the proper dosage of drugs, along with drug administration on an outpatient basis are discussed in relation to experiences in administering the anti-Parkinsonian drug, anatensol depot. With 17 patients taking this drug, success in changing administration to an outpatient basis was obtained in four cases, while five other cases showed significant progress when the drug was administered orally. It was also administered with some success to patients suffering schizophrenia. Success in outpatient administration was largely dependent on enlisting the aid of the family to make sure proper doses were continued even after some improvement in the patient's condition was evidenced.

000780 Tansella, Michele. Universita di Padova, Sede di Verona, Facolta di Medicina e Chirurgia, Verona, Italy **/Pharmacological therapy of insomnia./** La terapia farmacologica dell'insonnia. Rassegna di Studi Psichiatrici (Siena). 64(2):254-270, 1975.

Criteria for the rational treatment of insomnia in neurotic, depressed, and psychotic patients are presented. The prevalence of insomnia is demonstrated by case studies taken from the Los Angeles area. The misuse of pharmacotherapy in the treatment of insomnia is emphasized. A distinction is made between barbiturates (hypnotics) and euhypnics such as benzodiazepine and diazepam. While not as dependency and habit forming, euhypnics still need further study to determine their efficacy with regard to insomnia. 65 references.

000781 Tate, Douglas Lloyd. Carleton University Ottawa, Ontario, Canada **The effects of methylphenidate and thioridazine upon attention, arousal, and activity in mentally retarded youngsters. (Ph.D. dissertation).** Dissertation Abstracts International. 36(12):6424-B, 1976.

Theory and research on the nature of problems of hyperactivity, distractibility, and short attention span in normal and subnormal intelligence children were reviewed, and three studies compared the effects of methylphenidate and thioridazine on arousal, attention, and activity in mentally retarded subjects. It is argued that these problems represent a single dysfunction characterized as weak arousal in response to stimulation, and that the tranquilizers have a positive effect on the retarded as well as normal subjects. Although results of experiment 1 with hyperactive and retarded subjects were not significant, they provided some support for the arousal theory of hyperactivity and suggested possible beneficial and debilitative drug effects upon attention. Measures of reaction time, vigilance, and classroom behavior were made in experiments 2 and 3. Neither drug significantly altered any measure, but reaction time performance improved significantly over 5 weeks of testing. Results are discussed with reference to experimental design, drug dosages, S characteristics, and interaction between environmental and drug effects and reaction time deficits in the retarded. Further research on the use of psychotropic drugs in treating children's learning and behavior problems is recommended. (Journal abstract modified)

000782 Teravainen, Heikki; Larsen, Andreo. Dept. of Neurology, University of Helsinki, Haartmaninkatu 4, 00290 Helsinki 29, Finland **Effect of propranolol on acute withdrawal tremor in alcoholic patients.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 39(6):607-612, 1976.

The antitremor effect of the beta-adrenergic blocking agent propranolol was tested on 18 patients with a double-blind crossover method and with electrical recording of tremor amplitude and frequency during acute ithdrawal. The expected beneficial effect on the tremor during acute alcohol withdrawal did not occur. The central mechanisms in the acute phase may be of importance in producing the withdrawal tremor, on which propranolol is ineffective. 34 references. (Author abstract modified)

000783 Tigoli, F.; Rizzoli, G. Istituti Psichiatrici Provinciali di Cremona, Cremona, Italy **/Sleep deprivation and intravenous administration of Megimide as a means of EEG activation: a comparative clinical study./** La privazione di sonno e la somministrazione endovenosa di Megimide come mezzi di attivazione in elettroencefalografia clinica: studio comparativo. Rivista di Neuropsichiatria e Scienze Affini (Parma) 21(1):25-37, 1975.

The effects of sleep deprivation vs intravenous administration of Megimide on the EEG tracings were studied in epileptic patients who had no significant anomalies in EEG. The patients were divided into two groups: 28 males and 30 females, 15-53 years old, hospitalized for epileptic disorders, and a control group of 15 females and 11 males, 14-47 years old, hospitalized for neurotic behavior, but without epileptic tendencies. Both groups were under hospital care during 1972-73 and the EEG readings for all patients were made with an eight channel ECEM apparatus. Patients were forced to stay awake for 36 hours before new EEG tracings were made. Conclusions suggested that sleep deprivation was a useful technique in finding EEG anomalies in the epileptics but Megimide proved to be of little value in changing EEG tracings. 22 references.

000784 Tisdale, Samuel A., Jr.; Ervin, Dorothy K. A. H. Robins Company, Richmond, VA 23220 **Anorectic effectiveness of differing dosage forms of fenfluramine.** Current Therapeutic Research. 19(6):589-594, 1976.

An extended action dosage form of fenfluramine given once daily was compared for efficacy and toleration to idential doses of rapid release fenlfluramine dosed three times daily and to placebo in 286 overweight patients. For the two active drug forms, the incidence and type of side effect were similar, whereas the extended action form showed clear weight loss superiority over the 12 week trial. Tablets were significantly more efficacious than placebo. 6 references. (Author abstract modified)

000785 Vaisrub, Samuel. JAMA, 535 N. Dearborn St., Chicago, IL 60610 **The many faces of bromocriptine.** Journal of the American Medical Association. 235(26):2854-2855, 1976.

The potential usefulness of bromocriptine in a variety of clinical conditions is reviewed. Originally thought to be a stimulant to secretion of the hypothalamic prolactin-release inhibiting factor, the drug itself has since been shown to be such a factor, acting directly on the pituitary cells by activiating their dopamine receptors. Because this dopaminergic action is not confined to prolactin secreting cells, the drug (not yet approved for clinical use by the Food and Drug Administration) is being tried in the treatment of various disorders (puerperal lactation, galactorrhea, hypogonadism, hyperprolactinemia, infertility, acromegaly, and parkinsonism) that are susceptible to direct or indirect effects of dopamine receptor activation. Of particular interest is the effectiveness of bromocriptine in infertility associated with hyperprolactinemia and galactorrhea. Ovariani function can be regained by use of the drug so that

pregnancy becomes possible by stimulation of gonadotropins which had previously been blocked by prolactin. Bromocriptine has also been investigated for use in growth hormone problems, with encouraging results. The advantages of bromocriptine in a pharmaceutical sense (prompt action, relatively free of complications, and prolonged action) indicate its potential competition with levodopa in treatment of parkinsonism. Clinical trials in cases of infertility, acromegaly, and parkinsonism appear successful. 7 references.

000786 Varkonyi-Wallerstein, Paul; Licht, B.; Kronenwerth, D. II. Geriatrische Klinik Sonnenberg, D-6600 Saarbrucken, Germany **/Treatment of cerebral insufficiency symptoms in the elderly: randomized comparative study of Trivastal./** Zur Behandlung zerebraler Insuffizienzerscheinungen alter Menschen; Randomisierte Vergleichsprufung mit Trivastal. Therapie der Gegenwart (Munchen). 115(2):265-266, 269-270, 272-274, 276-278, 280, 1976.

The effect of piribedil (Trivastal) on cerebral insufficiency syndrome was studied in a group of 40 geriatric patients. Trivastal lowers blood viscosity, increases utilization of glucose and oxygen, raises cerebral perfusion pressure, corrects acidosis, improves microcirculation, and raises resistance to endogenous and exogenous disorders. The patients were randomly assigned to two groups, one of which received Trivastal in addition to the regular cardiovascular therapy. No other drugs administered had the same action as Trivastal. Results were evaluated on the basis of clinical findings, laboratory tests, EEG, and psychological tests. Results showed that in the test drug group there was definite improvement in six cases, moderate improvement in three, moderate improvement in six, no improvement in eight, and deterioration in three patients of the regular treatment group. 15 references.

000787 Voller, G. W. Elena-klinik, Klinikstrasse 16, D-3500 Kassel-Harleshausen, Germany **/Parkinson's syndrome: drug therapy./** Parkinson-Syndrom: Medikamentose Therapie. Paracelsus (Wien). No. 9/10:241-243, 1975.

The treatment of Parkinsonism with anticholinergics, L-dopa, and amantadine derivatives is discussed. The anticholinergics are more effective in treating the rigor of Parkinsonism than the tremor. They have a latency of effect of 2 weeks. Side-effects are delirium, inhibited micturition, increased convulsive threshold, glaucoma, disturbances in accommodation, and dry mouth. The use of L-dopa is based on the fact that in Parkinsonism there is a lack of dopamine in certain extrapyramidal motor centers. The daily dose of L-dopa is slowly raised until an optimal level is reached. Side-effects are nausea and vomiting, hypotension, disturbances of cardiac rhythm, hyperkinesia and dyskinesia, agitation, mental symptoms, and sensory disturbance. Contraindications are history of psychosis or neurosis, pregnancy, or decompensation of the cardiac, renal, hepatic, endocrine, or hematopoietic systems. Contraindications for sympathomimetic amines also apply to L-dopa. L-dopa should not be used with sympathomimetic amines or anesthesia. The combination of L-dopa with decarboxylase inhibitors is discussed. The amantadine derivatives affect the symptoms of rigor, tremor, and akinesia, but to a lesser degree than does L-dopa.

000788 Wada, Juhn A.; Sato, Mitsumoto; Wake, Akira; Green, John R.; Troupin, Allan S. Division of Neurological Sciences, Faculty of Medicine, Univ. of British Columbia, Vancouver, Canada **Prophylactic effects of phenytoin, phenobarbital, and carbamazepine examined in kindling cat preparations.** Archives of Neurology. 33(6):426-434, 1976.

Prophylactic effects of phenobarbital, phenytoin (diphenylhydantoin), and carbamazepine were examined in amygdaloid kindling preparations in cats. Daily electrical stimulation was delivered at the time of peak plasma levels. Comparative examination of the chronological pattern of the clinical seizure development, after discharge growth, and formation of distant independent spike foci was made between periods of kindling with chronic drug administration and of re-kindling without drugs. Both phenobarbital and carbamazepine were effective, but phenytoin was totally ineffective. Prophylactic action of phenobarbital and carbamazepine was mainly through the suppression of the development of motor seizure manifestations in the former and the same with the development of sustained afterdischarge in the latter. The kindling preparation appears to possess many desirable features as an ideal model of human epilepsy for the purpose of assessment and recruitment of potential antiepileptic drugs and development of a rational pharmacotherapeutic approach for the management and prevention of seizure disorder. 32 references. (Author abstract)

000789 Waltregny, A.; Dargent, J. Stereotactic and Functional Neurosurgery Section, Neurosurgical Clinic, University of Liege, Belgium **Preliminary study of parenteral lorazepam in status epilepticus.** Acta Neurologica Belgica (Bruxelles). 75(5):219-229, 1975.

The use of parenteral lorazepam (Temesta) in the acute treatment of 11 patients with confirmed status epilepticus is studied. Ten adults and one 6-year-old child were injected respectively with 5mg and 2.5mg lorazepam. Diazepam was also administered as a second dose to two of the subjects. Electroencephalographic study (ten-twenty system) was performed before, during and 5-10 min after the injection with lorazepam for a thorough assessment of effects. The quantitative analysis was presented as a histogram of the tracings showing the time span of the paroxysmal discharge and expressed as a percentage per minute. Results show that all of the patients exhibited prompt cessation of seizures both electrical and clinical. Some data indicate a longer lasting relief than that provided by an equal dose of diazepam. 9 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

000790 Benedetti, Gaetano. no address **/Selected essays on schizophrenia./** Ausgewahlte Aufsatze zur Schizophrenielehre. Gottingen, Vandenhoeck & Ruprecht, 1975. 232 p. DM 38.

A selected collection of writings on schizophrenia is presented. Psychodynamics and psychotherapy of schizophrenia receive special attention. Topics covered include LSD intoxication, failure of ego functioning, the superego in schizophrenia, the haziness of drive development, disintegration and fragmentation of the ego, psychotherapy of the schizophrenic, psychogenesis of schizophrenia, and loss of ego boundaries. Psychodynamics becomes the link between the unknown biological cause and the descriptive psychotic syndrome.

000791 Cade, C. Maxwell; Gauld, Alan; Hart, Ann Woolley; Rowan, John. no address **Symposium on altered states of consciousness.** Bulletin of the British Psychological Society (London). 28:241, 1975.

The background on research into altered states of consciousness and a brief survey of recent developments are presented, followed by a detailed discussion of biofeedback in the self-regulation of internal states and the influence of

psychedelic drugs on such states. Topics include the psychophysiological principle, biofeedback with and without instruments, controllable and uncontrollable states of consciousness, group teaching of self-regulation, meditation and deep psychophysiological relaxation, and the effect of such relaxation on the nervous system. The clinical, conventional, mystical and excessive approaches to the use of LSD are outlined and the importance of this drug to humanistic psychology is suggested. Current investigations with LSD are reviewed and some personal experiences with it are described. The relationship between extrasensory perception and altered states of consciousness is explored in terms of recent research. (Author abstract modified)

000792 Feinberg, Irwin; Jones, Reese; Walker, James; Cavness, Cleve; Floyd, Thomas. Psychiatric Service, Veterans Administration Hospital, 4150 Clement Street, San Francisco, CA 94121 **Effects of marijuana extract and tetrahydrocannabinol on electroencephalographic sleep patterns.** Clinical Pharmacology and Therapeutics. 19(6):782-794, 1976.

The effects of marijuana extract and tetrahydrocannabinol on electroencephalographic sleep patterns was studied to ascertain whether physiological and behavioral effects of the pure drug and of the natural constituents of the plant differ from those produced by tetrahydrocannabinol alone. Since it was found that tetrahydrocannabinol in high dosage induced alterations of electroencephalographic sleep patterns, a determination was made whether marijuana extract containing the same amount of tetrahydrocannabinol and administered under the same conditions would induce the same or different effects. It was found that marijuana extract, given in daily doses containing 70-210mg delta-9-tetrahydrocannabinol, induced effects on sleep which are virtually identical to those produced by the same doses of relatively pure (96%) tetrahydrocannabinol. Both drugs reduced eye movement density with some tolerance developing to this effect. Stage 4 tended to increase with drug administration. Abrupt withdrawal led to high densities of eye movement, increased rapid eye movement durations, and a sharp, transient fall in stage 4 to baseline levels. Implications of the research findings with respect to psychopharmacology of unipolar and bipolar depressed patients are discussed. 23 references. (Author abstract modified)

000793 Friedhoff, Arnold J.; Schweitzer, Jack W. Millhauser Laboratories of the Department of Psychiatry, New York University Medical Center, New York, NY **Mammalian biosynthesis of potential psychotogens derived from dopamine.** In: Friedhoff, A., Catecholamines and behavior. Vol. 1. New York, Plenum Press, 1975. 235 p. (p. 187-200).

A summary is presented of the investigations into the mammalian enzymes that can catalyze the formation of methylated hallucinogenic derivatives of biogenic amines. The methylation hypothesis of schizophrenia suggests that psychotics may be capable of synthesizing one or more psychotogens by excessive or abnormal methylation, using as substrates structurally related biogenic amines or their normal metabolites. The di-O-methylated derivative of dopamine, 3,4-dimethoxyphenethylamide (DMPEA) exhibits biochemical effects on dopamine pathways, and behavioral effects inducing hypokinetic syndromes such as catatonia when injected into animals. In a discussion of the aspects of biological O-methylation, the alteration of the activity of the enzyme catechol-O-methyltransferase (COMT) is shown to be associated with schizophrenia, Down's syndrome and affective disorders. In a study of o-methylating enzymes capable of forming hallucinogens, a variety of guaiacol substrates were tested with an enzyme designated guaiacol-o-methyltransferase (GOMT). The methylation of phenolic trioxy precursors of mescaline and its metabolites is investigated. An alternative to the transmethylation hypothesis, namely that certain endogenous hallucinogens serve a normal function and that exogenously administered mescaline produces psychotic manifestations because it disrupts this normal function, is presented.

000794 Khorramzadeh, E.; Lotfy, A. O. Department of Psychiatry, Pahlavi University School of Medicine, Shiraz, Iran **Personality predisposition and emergence phenomena with Ketamine.** Psychosomatics. 17(2):94-95, 1976.

A study of Ketamine was conducted to determine the type of emergence phenomenon reportly observed when used as an anesthetic, and to discover any correlation between these reactions and the type of personalities involved. Preoperative patients (n=606) were given a questionnaire to determine the three dimensions of personality extraversion, neuroticism and psychoticism. After Ketamine administration, observations showed 35% had psychotomimetic reactions; 8% had unpleasant side effects. These 8% belonged to the group whose personality inventories were rated high in psychoticism. The results did not contraindicate Ketamine's use as an anesthetic. 6 references.

000795 Maugh, Thomas H., II. no address **Marihuana: new support for immune and reproductive hazards.** Science. No. 4217:865-867, 1975.

A summary of some recent research results on immune and reproductive hazards of marihuana smoking is considered in light of expanding pressure for decriminalization. Research on cannabis has generally been characterized by a great number of inconsistencies and contradictions, with workers from different laboratories often reporting widely differing results. The major problem with all of the findings based on work with animals or cultured cells is extrapolating them to humans. There is a little evidence, such as that presented by Kolodny, that some long-term cannabis users suffer from sexual impotence and infertility, but there is no evidence of any widespread occurrence of this phenomenon in either the U.S. or foreign cultures where cannabis use is even more common. Similarly, there is no evidence for an increased incidence of infectious diseases or cancer among these populations, as would be expected if there were an impairment of immunity. There is, however, also no evidence that such effects are not occurring.

000796 Peters, B. A.; Lewis, E. G.; Dustman, R. E.; Straight, R. C.; Beck, E. C. Neuropsychology Research Laboratories, Veterans Administration Hospital, Salt Lake City, UT 84113 **Sensory, perceptual, motor and cognitive functioning and subjective reports following oral administration of delta9-tetrahydrocannabinol.** Psychopharmacology (Berlin). 47(2):141-148, 1976.

Three dose levels, 0.2, 0.4, and 0.6mg/kg, of delta9-tetrahydrocannabinol (THC) and a placebo were orally administered to 10 frequent and 10 occasional marijuana users to evaluate the effects on affective and somatic sensations. Following ingestion of each dose and the placebo, objective tests selected from a battery of sensory and perceptual motor tests routinely used to evaluate cerebral dysfunction in hospitalized patients were administered. The influence of delta9-THC on proficiency and variability of performance was minimal. However, when individual test scores and variabilities were combined and converted to standard scores, allowing for analysis of overall performance, THC had a small but consistent detri-

mental effect on both proficiency and variability of performance. In contrast, THC exerted profound effects on the subjective experiences of the volunteers as addressed by the Subjective Drug Effects Questionnaire. Subjective changes in mood, feeling, perception and somatic sensations were reported by all subjects but were more pronounced in the occasional user group. It was proposed that the small impairment noted in objective test performance after ingestion of delta9-THC as contrasted to the large effects on subjective responses suggests that the principal effects of marijuana are on the autonomic nervous system rather than on higher cortical functions. 49 references. (Author abstract modified)

000797 Zinberg, Norman E. Cambridge Hospital of Harvard Medical School, Cambridge, MA 02138 **Observations on the phenomenology of consciousness change.** Journal of Psychedelic drugs. 8(1):59-76, 1976.

An essay on consciousness changes, specifically high states, presents discussion of the following: the language; the social contexts including analysis of the psychotomimetic effects of opiates and psychedelic drugs; the mental set and the setting as separate influences; a theoretical framework for the concept of consciousness; Timothy Leary's role as counterculture priest; the legal and ideological reaction plus the mental health center appraisal of psychotic symptoms from psychedelic drugs; the relativism to American cultural and historical perspectives on drug habits; the dominant influence of Freud, particularly on the dream state and his prevailing effect on subsequent research; distinction between primary process thinking and secondary process thinking; the hierarchy of awareness and consciousness changes; clinical interviews with 34 psychedelic users who controlled or altered the expected pharmacological action, of LSD, mescaline, marijuana, etc.,demonstrating indications of increased empathic awareness and insight; an assessment of whether drug use permanently changes basic personality and/or contributes to small shifts in personality reorientation. It is recommended that in studying drugs effects, the user, the researcher, and the society be studied as well as the drug, because each pattern of drug use constitutes a distinctive mode or quality of alternate state experience. In training, researchers are encouraged to induce altered states of consciousness via drugs for studying perception and attention processes. 56 references.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

000798 Andreasen, P. B. no address **Pharmacokinetics of sedatives in liver disease.** European Journal of Clinical Pharmacology (Amsterdam). 10(2):115, 1976.

The biochemical action of diazepam, prescribed as a sedative for patients with cryptogenic or alcoholic cirrhosis, was studied in nine patients and in four others without liver disease. Subjects received a fixed 10mg dose administered intravenously over a period of 5 min. The mean biological half life of the drug was five times greater in cirrhosis patients than in the controls (164 hr versus 32.1hr). Mean plasma clearance was 17.1ml/min in the former and 35 ml/min in the latter. This clearance could be correlated neither with a quantitative measure of liver function, nor with semiquantitative measures. This may indicate that the plasma clearance of diazepam is an inaccurate index of its hepatic metabolism rate, possibly due to the drug's complex kinetics.

000799 Andresen, B. D.; Templeton, J. L.; Hammer, R. H.; Panzik, H. L. College of Pharmacy, University of Florida, Gainesville, FL 32610 **Synthesis and characterization of a catechol metabolite of glutethimide (Doriden) in human urine.** Research Communications in Chemical Pathology and Pharmacology. 14(2):259-268, 1976.

A metabolite of glutethimide, 2-ethyl-2-(3,4-dihydroxyphenyl)-glutarimide, previously identified in enzymatically hydrolyzed human urine of overdosed victims was prepared synthetically and its chemical and spectral data compared to the proposed material. Results of these comparisons confirm the presence of a catechol metabolite of glutethimide in the urine of patients severely intoxicated by the parent drug. 14 references. (Author abstract)

000800 Bengesser, G. Wagner Jauregg Krankenhaus, Wagner Jauregg Weg 15, A-4020 Linz, Austria **/Comparison of EEG and clinical findings in Parkinson patients receiving L-dopa./** Vergleich zwischen EEG-Befund und klinischem Bild bei Parkinson-Patienten unter L-Dopa. Wiener Medizinische Wochenschrift (Wien). 125(7/8):120-121, 1975.

In a study of the pathophysiology of Parkinson's disease the EEG was studied in 53 patients receiving L-dopa therapy over a period of 3 months to 4 years. Total clinical improvement among these patients was about 60%. Before commencement of L-dopa treatment 26 of the 53 patients showed abnormal EEG. Following 6 weeks of treatment 9 patients showed an improved EEG. Long-term observation showed the EEG improvement consisted of regularization of alpha waves in 28 cases, and a decrease in slow waves in 11 cases. EEG deterioration was noted in 28 cases, and in 26 of these was correlated with clinical deterioration. There was no correlation of clinical findings with EEG pattern before L-dopa treatment. L6 references.

000801 Bergonzi, P.; Chiurulla, C.; Gambi, D.; Mennuni, G.; Pinto, F. Clinica delle Malattie Nervose e Mentali, Universita Cattolica del S. Cuore, Rome, Italy **L-dopa plus dopa-decarboxylase inhibitor: sleep organization in Parkinson's syndrome before and after treatment.** Acta Neurologica Belgica (Bruxelles). 75(1):5-10, 1975.

To examine the effects of L-dopa plus dopa-decarboxylase inhibitor on sleep organization of patients affected by Parkinson's syndrome, 64 all-night sleep polygraphic and EEG recordings were carried out before and after treatment with this combination. Eight patients (five female, three male) ranging in age from 40-60 years participated in the study. The parameters characterizing sleep patterns were quantified, i.e. absolute and percentage occurrence of wakefulness and sleep stages, as well as the trend and duration of Kleitman's cycles. Results indicate that without any drug, Parkinsonian patients showed sleep disruption with frequent awakenings, reduction of total sleeping time and lessening of REM stage rather than slow sleep. Treatment with L-dopa plus inhibitor appeared to be able to restore good night sleep organization with a noteworthy increase in the REM stage. These results tend to confirm those obtained during animal research regarding the importance of catecholamines in triggering REM sleep. 17 references. (Author abstract modified)

000802 Bieniowa, Anna; Kolasa, Maria; Reichowa, Janina. Klinika Neurologiczna, ul. Botaniczna 3, 31-501 Krakow, Poland **/L-dopa treatment in Parkinsonism. Biochemical basis./** Leczenie Parkinsonizmu L-dopa. Podstawy biochemiczne. Przeglad Lekarski (Warszawa). 33(4):463-467, 1976.

The mechanism action of L-dopa in Parkinsonism is analyzed on the basis of a review of several studies. The steps

in catecholamine synthesis and the reaction of cholinergic and adrenergic systems to drugs used in the treatment of Parkinsonism are outlined. It has been observed that the dopamine content of the basal ganglia in the brain is significantly decreased in Parkinsonism, and that 70-80% of Parkinsonism cases recover following L-dopa treatment. A number of side-effects have been observed, such as methylation inactivation of catechol compounds. Chemotherapeutic inhibition of this has had varying degrees of success, but further research is indicated. 18 references.

000803 Bleiweiss, Herman. Universidad Nacional de Buenos Aires, Buenos Aires, Argentina /**Minimal brain damage syndrome (chromosomal changes and lithium treatment).**/ Sindrome de disfuncion cerebral minima (alteraciones cromosomicas que presenta y su tratamiento con litio). Neuropsiquatrica (Buenos Aires). 6(1):30-35, 1975.

Distinction between genetic and chromosomal anomalies in minimal brain damage syndrome and suggestions for altering traditional therapeutic approaches are made. Psychiatric and physical examinations, including an electroencephalogram and a chromosoaml test, were given to a group of 34 patients, between ages 3 and 22, who had previously been under treatment. Seven patients were found to have chromosomal abnormalities. In each case, highly aggressive and hyperactive behavior was observed. Patients were treated with daily doses between 25mg to 100mg of lithium carbonate, and between 10mg and 100mg of thioridazine. After 1 week, lithium was prescribed exclusively. In most cases, medication was suspended after 1 year. Prior to that, termination of medication led to reappearance of symptoms within 8 to 10 days. It is postualted that the advantage of using drugs to treat children and adolescents is that they control aggression, facilitate learning and ability to concentrate, and increase the patient's awareness of his illness. 5 references.

000804 Borg, Karl Olof; Carlsson, Enar; Hoffmann, Kurt-Jurgen; Jonsson, Tor-Erik; Thorin, Hans; Wallin, Boel. Department of Analytical Chemistry and Biochemistry, AB Hassle, Fack, S-431 20 Molndal, Sweden **Metabolism of metoprolol-(3H) in man, the dog and the rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):125-135, 1975.

The main urinary metabolites of metoprolol-(3H) in man, the dog and the rat were identified by gas chromatography and mass spectrometry by comparison with synthesized reference compounds. The amounts of the different metabolites in urine were determined by radio/gas chromatography. In man metoprolol was metabolized by oxidative deamination, O-dealkylation with subsequent oxidation and aliphatic hydroxylation into 3 main urinary metabolites which together accounted for 85% of the total urinary excretion. In the dog and the rat the same metabolites could be recovered but in different relative abundances. The inhibition of cardiovascular effects of isoprenaline by the metabolites and a presumed metabolite was studied and compared with the effects of metoprolol. Two of the compounds blocked the isoprenaline responses but they were 2 to 8 times less potent than metoprolol. The metabolites showed a significantly lower acute toxicity in mice than metoprolol. 10 references. (Author abstract)

000805 Bortolotti, M.; Sanavio, C.; Sansone, G.; Labo, G. no address **Actions of sulpiride on gastric motility and acid secretion in duodenal ulcer patients.** Medicina Psicosomatica (Roma). 20(4):427, 1975.

A study of the effects of intravenous administration of 1.5mg/Kg Sulpiride on gastric motility and acid secretion in 22 duodenal ulcer patients was reported at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Results showed that: 1) sulpiride inhibits acid response to pentagastrin and stimulates a propulsive motility in the human stomach; 2) the effect of motility is more important than the effect on acid secretion; and 3) the motor effect is attained through extravagal pathways. (Author abstract modified)

000806 Boulenger, J.-P.; Brion, S. Centre Hospitalier de Versailles, 1, rue Richaud, F-78000 Versailles, France /**Mode of action of lithium in manic-depressive psychosis: a few present day methods of research.**/ Mode d'action du lithium dans la psychose maniaco-depressive: a propos de quelques voies actuelles de recherche. Encephale (Paris). 2(2):153-165, 1976.

Research techniques in elucidating the mode of action of lithium in manic-depressive psychosis are discussed. The areas discussed are: clinical data, behavioral effects in the animal, action on neurotransmitters (monoamines, acetylcholine, amino acids), action of lithium on electrolytes, and miscellaneous actions, e.g. on cyclic AMP, on enzymic systems, on the EEG, on biological rhythms, and on the fetus. It is suggested that the therapeutic action of lithium salts on manic states is related to its action on cerebral receptors decreasing the available norepinephrine. This decrease would correspond to the aminergic theory of affective disorders. 73 references.

000807 Bruun, Ruth D.; Shapiro, Arthur K.; Shapiro, Elaine; Sweet, Richard; Wayne, Henriette; Solomon, Gail E. 52 East 73rd Street, New York, NY 10021 **A follow-up of 78 patients with Gilles de la Tourette's syndrome.** American Journal of Psychiatry. 133(8):944-947, 1976.

In order to evaluate the effects of chemotherapeutic treatment, the followup study of 78 patients with Gilles de la Tourette's syndrome was conducted. Four of the patients were in spontaneous remission; 59 patients taking haloperidol showed an average improvement of 79.3%; and the remaining patients, three of whom were taking medication other than haloperidol and 12 of whom were not taking any medication, showed an average improvement of 24.7%. Side-effects were the main cause of discontinuing haloperidol. Response to haloperidol was unrelated to family history of tics, age at onset, type or severity of symptoms, or signs of organicity. 12 references. (Author abstract modified)

000808 Caruthers, S. G.; Kelly, J. G.; Johnson, G. W.; McDevitt, D.G.. Department of Therapeutics and Pharmacology, Queens University of Belfast and the Royal Victoria Hospital, Belfast, Northern Ireland **Biliary excretion and enterohepatic recirculation of practolol in man.** Irish Journal of Medical Science (Dublin). 145(6):187-194, 1976.

The elimination of practolol in bile was studies in six patients who received a single oral dose of 400mg within six days undergoing biliary surgery. There was wide variation in the concentration of practolol in bile and in the total amount of practolol excreted in bile during the 48 hours period after dosage. Two patients excreted 23% and 41% of the 400mg mg dose in bile, whereas the excretion in the other four patients was only 1% to 4% of the oral dose. The total elimination ranged from 92% to 105% in four of the patients. The mean elimination half-life in normal subjects receiving the same practolol dose. Since complete or near complete urinary excretion of practolol is found in normal subjects, the presence of large amounts of drug in the bile suggests that enterohepatic recirculation of the drug occurred in some of the patients at least. This is a possible explanation of the shortened half-life

in these patients in whom drug was being removed with bile. The four patients with low excretion of practolol in bile were receiving other drugs at the time of the study. These included nitrazepam, diazepam and tetracycline which are known to have substantial biliary elimination either in animals or man. It is suggested that competition for biliary excretion may have occurred and this may represent a drug interaction of possible clinical significance. 14 references. (Author abstract modified)

000809 Clouet, Doris H. Testing and Research Laboratory, New York State Drug Abuse Control Commission, Brooklyn, NY **Possible roles of catecholamines in the action of narcotic drugs.** In: Friedhoff, A., Catecholamines and behavior. Vol. 2. New York, Plenum Press, 1975. 225 p. (p. 167-196).

The studies of the relation between brain catecholamines and pharmacological responses induced by morphine and other narcotic analgesics are reviewed. The predominant responses are dependent on the dose used and the species investigated as are the potency and duration of activity of each drug. The opiate antagonists are nalorphine, levallorphan and naloxone, and the narcotic antagonists are morphine, levorphavol, etorphine, heroin, meperidine and methadone. The mechanism of the development of tolerance to chronic exposure to these drugs is discussed. The results of experiments on the effects of MAO inhibitors, tricyclic antidepressants, adrenergic blocking agents, amine depletors, inhibitors of catecholamine synthesis, amphetamines and cocaine, catecholamines and their precursors, neuroleptics, apomorphine, amantadine and 6-hydroxydopamine on opiate activity are described. The alteration in brain catecholamine levels, turnover rate, and transport produced by acute or chronic administration of morphine and other opiates are explained. The effects of opiates on the cyclic AMP/adenge cyclase system are discussed. The implications of these studies have been formulated into a dopamine receptor hypothesis in which manifestations of opiate induced activity are associated with striatal dopamine metabolism. It is postulated, however, that while brain catecholamines are involved in the mechanism of opiate action and dependence, the operation of this single neurotransmitter cannot alone be responsible for these mechanisms. 168 references.

000810 Culebras, Antonio. Neurologia, Fundacion Jimenez-Diaz, Avenida Reyes Catolicos 2, Madrid, Spain **Effect of papaverine on cerebral electrogenesis.** Neurology. 26(7):673-679,1976.

A double-blind, placebo controlled study was conducted in 20 elderly patients with dementia associated with diffuse cerebrovascular disease to determine the effects of papaverine on the electrical activity of the brain. Frequency spectrum analysis of electroencephalograms show that papaverine decreases mean electrical content of the delta/theta band (0Hz to 7.5Hz) significantly and increases mean electrical content of the alpha band (7.6Hz to 12.5Hz) significantly from baseline. The correlation between changes in the clinical conditions of the patients and changes in EEG activity was also examined; however, correlations between improvements in signs and symptoms and decreases in delta/theta activity were not apparent in all patients. It is suggested that papaverine favorably affects neuronal metabolism, possibly through improved perfusion of the tissue, although the exact mechanism of action remains unknown. 11 references. (Author abstract modified)

000811 Curry, S. H.; Evans, S. Dept. of Pharmacology & Therapeutics, London Hospital Medical College, Turner Street, London E1 2AD, England **A note on the assay of chlorpromazine N-oxide and its sulphoxide in plasma and urine.** Journal of Pharmacy and Pharmacology (London). 28(5):467-468, 1976.

In a contribution to the knowledge of the presence of amine analogues of chlorpromazine in biological fluids, assay methods of chlorpromazine-N-oxide (CPZNO) and chlorpromazine-N-oxide-sulfoxide (CPZNOSO) are described and conducted on samples of plasma and urine. The samples were heparinized plasma (by venepuncture), and urine, from: 10 acutely treated, responding schizophrenics previously untreated receiving 100mg chlorpromazine 3 times daily for 36 days, samples being collected throughout the 36 days; 8 patients undergoing long-term treatment (more than 6 months) at low doses (20mg to 25mg 3 times daily); and 20 patients during and after long-term treatment (more than 2 years) at higher doses (50mg to 200mg, 3 times daily). All plasma samples were collected just before or 2-4 hr after routine oral doses of chlorpromazine. Urine samples were taken at 24 hr intervals. Gas chromatography was used. 8 references.

000812 Danielsen, A.; Haffner, J. F. W.; Morland, J.; Setekleiv, J.; Frivik, P. T.; Stromsaether, C. E. Psychological Service of the Norwegian Armed Forces, Norway **Effects of diazepam and ethanol on heart rate and galvanic skin responses.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(2):113-122, 1975.

Heart rate (HR), heart rate variability (HRV), and the amplitude and frequency of galvanic skin response (GSR) were studied in nine healthy young males 2-3 hours after oral administration of either placebo, diazepam (10 and 20mg/70kg body weight), ethanol (0.78 and 1.22ml/kg), or combined administration of diazepam (10mg) and ethanol (0.78ml/kg). When examinations were performed in resting subjects, ethanol produced significant increases in heart rate, as did combined administration of ethanol and diazepam. Heart rate variability, supposedly correlated to reaction time, was reduced by combined administration of the two drugs. The frequency of the GSR was reduced by both ethanol and 20mg diazepam, although not significantly, and was reduced on one occasion by ethanol. Stimulation by mental arithmetic increased all parameters, and more so after drug treatment than after placebo. The results are discussed in relation to the possible effects of diazepam on the autonomic nervous system, and also in relation to the psychophysiological activation theory which presupposes that increased activation is related to increased sympathetic activity. It is concluded that the parameters used are not reliable as indicators of whether a drug is deactivating or not. 17 references. (Author abstract)

000813 Davis, John M. Illinois State Psychiatric Institute and University of Chicago, Pritzker School of Medicine, Chicago, IL **Catecholamines and psychosis.** In: Friedhoff, A., Catecholamines and behavior. Vol. 2. New York, Plenum Press, 1975. 225 p. (p. 135-154).

A review of the evidence on the dopaminergic theory of schizophrenia arising from human studies is presented, and research into pharmacologic mechanisms of amphetamine psychosis is integrated with the clinical effects of amphetamines in man. Amphetamine induced paranoid psychosis, indistinguishable from schizophrenia, appears following high dose amphetamine ingestion, but clears within several days of discontinuing amphetamine. This psychosis is considered the result of the amphetamine itself, and possibly the false transmitters hydroxynorephedrine and norephedrine. Psychomotor stimulants (e.g. methylphenidate) are shown to exacerbate psychoses, presumably mediated by dopamine. The

effect of physostigmine in antagonizing psychoses activation by methylphenidate is investigated to clarify whether psychotic behavior is controlled by a balance between transmitters or by a single transmitter. The study indicated a transmitter balance controlling the worsening properties of drug psychosis. A two factor alternative to the dopamine theory is suggested on the basis of the research. The alternative theory hypothesizes that factor one is the "turning on" of schizophrenia (a process whose mechanism still needs definition) and that factor two is the dopamine mediated stimulation or "turning up" of schizophrenia. 93 references.

000814 de Sagher, R. M.; De Leenheer, A. P.; Claeys, A. E. Faculteit van de Farmaceutische Wetenschappen, Rijksuniversiteit, Academisch Ziekenhuis, 135 De Pintelaan, 9000 Gent, Belgium **Identification and quantitative GLC determination of iproniazid in human urine.** Journal of Pharmaceutical Sciences. 65(6):878-882, 1976.

A GLC (gas/liquid chromatography) method for the specific identification and quantitation of iproniazid, a potent monoamine oxidase inhibitor drug, is described. The free drug is isolated from urine samples by two phase extraction reinforced with salting out. Identification and quantitative determination at the microgram level are done on aliquots of the choloroform extract by GLC, using the 2-butyl analog as an internal standard. Iproniazid and potentially interfering compounds present in the extracts are also identified by GLC mass spectrometry and thin layer chromatography for supporting evidence of the GLC method's specificity. 13 references. (Author abstract modified)

000815 Deniker, P.; Loo, H.; Zarifian, E.; Bousquet, B.; Dreux, C.; Escande, C. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, Hopital Saint-Anne, 1, rue Cabanis, Paris, France **/Study of free and total tryptophan in plasma. Its interest in psychiatry./** Etude du tryptophane libre et total dans le plasma. Son interet en psychiatrie. Encephale (Paris). 2(2):123-131, 1976.

Total tryptophan and free tryptophan were measured in the plasma of normals and of schizophrenics. The values obtained in 16 normal subjects not taking any drugs were 1.45-2.80mg/l of free tryptophan and 7.35-14.95mg/l of total tryptophan. Values of tryptophan were then obtained in 12 schizophrenics, 5 males and 7 females, ranging in age from 21 to 51. In the five schizophrenics who were not being treated, the values of free and total tryptophan did not differ from normal. Also in the three schizophrenics on chlorpromazine, the values of free and total tryptophan were within the normal range. The one patient on pipothiazine had a normal total tryptophan and a slightly elevated free tryptophan. Of the three patients on lithium, two had high normal or elevated total and free tryptophan levels, and one had normal values. 19 references.

000816 Duret-Cosyns, S.; Samain, W. no address **/Research on the use of sulpiride in psychosomatic medicine: a study of 104 cases./** Recherche sur le sulpiride en medecine psychosomatique -- etude de 104 cas. Medicina Psicosomatica (Roma). 20(4):428, 1975.

Use of sulphiride in psychosomatic therapy was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Psychopharmacological therapy of 104 patients suffering from single or associated somatic symptoms followed by psychological tests showed that: 1) sulpiride was well toleratted in most cases; 2) its action was beneficial to the patient; 3) certain somatic problems responded well to treatment, especially those of a digestive and cardiovascular nature; and 4) antidepressant effect was noted as well as the emotionally stabilizing factor, especially in relation to neurovegetative equilibrium.

000817 Estler, C.-J. Institute of Psychopharmacology, University of Erlangen-Nurnberg, Erlangen, Germany **Effect of amphetamine-type psychostimulants on brain metabolism.** Advances in Pharmacology and Chemotherapy. 13:305-357, 1975.

In a continuing series of reports on advances in pharmacology and chemotherapy, the literature on the effect of amphetamine type psychostimulants on brain metabolism is reviewed. Behavioral changes, electroencephalogram, amphetamine levels in the central nervous system, cerebral function, and brain metabolism are covered. While the mode of the psychostimulatory action of the amphetamine type psychostimulants is still not clear, the majority of observations favors the view that amphetamine and methamphetamine act through an indirect sympathomimetic mechanism in which adrenergic and/or dopaminergic receptors are involved. The hyperkinetic effect of the drugs seems to be dependent on the availability of newly synthesized norepinephrine and/or dopamine. It appears that dopaminergic mechanisms are involved in the stereotyped movements that supposedly originate from stimulation of the extrapyramidal motor system. 318 references.

000818 Fann, William E.; Lake, C. Raymond. Baylor College of Medicine, Texas Medical Center, Houston, TX 77025 **Amantadine versus trihexyphenidyl in the treatment of neuroleptic-induced parkinsonism.** American Journal of Psychiatry. 133(8):940-943, 1976.

In order to determine the effectiveness of amantadine, a putative dopaminergic compound, on drug induced Parkinson's disease, a double-blind placebo controlled crossover study of 39 psychiatric inpatients was conducted. Amantadine and trihexyphenidyl were found to be equally effective in treating drug induced parkinsonism, and amantadine produced fewer and less severe side-effects. It is suggested that amantadine is an effective alternative to atropine like agents, with fewer implications for long-term risk of tardive dyskinesia. 10 references. (Author abstract modified)

000819 Fink, Max; Irwin, Peter; Weinfeld, Robert E.; Schwartz, Morton A.; Conney, Allan H. Department of Psychiatry, Health Sciences Center, SUNY, Stony Brook, NY 11790 **Blood levels and electroencephalographic effects of diazepam and bromazepam.** Clinical Pharmacology and Therapeutics. 20(2):184-191, 1976.

The question of whether diazepam per se possesses pharmacologic activity, or whether its activity depends upon its N-desmethyl metabolite is examined. The data indicate that diazepam exerts a pharmacologic effect on the electroencephalograph (EEG) in the absence of measurable N-desmethyldiazepam in the blood, arguing that diazepam does possess pharmacologic activity. Another indication that diazepam possesses pharmacologic activity is that rapid anticonvulsant and sedative effects occur shortly after an intravenous dose of diazepam before measurable blood levels of N-desmethyldiazepam are reached. Both drugs caused an increase in beta activity and a decrease in alpha activity. 20 references

000820 Gerlach, J.; Thorsen, K. Sct. Hans Hospital, Dept. E, DK-4000 Roskilde, Denmark **The movement pattern of oral tardive dyskinesia in relation to anticholinergic and antidopaminergic treatment.** International Pharmacopsychiatry (Basel). 11(1):1-7, 1976.

Twenty four hospitalized psychiatric patients with neuroleptic-induced oral tardive dyskinesia were treated with alpha-methyl-para-tyrosine (AMPT), 4g daily for 3 days, and biperiden, an anticholinergic 12mg daily for 3 weeks. The results were evaluated blindly by means of videotape technique. The frequency of tardive dyskinesia was significantly reduced by AMPT and significantly increased by biperiden. The amplitude was reduced by AMPT in ten cases, unchanged in 12 cases and increased in two cases. Biperiden significantly increased the amplitude. The duration of each separate tongue protrusion and/or mouth opening was significantly increased by AMPT and reduced or unchanged by biperiden. It is concluded that a reduced dopaminergic activity (pharmacological or organic) may constitute the primary pathogenetic background for tardive dyskinesia, but that dopaminergic hypersensitivity and/or cholinergic hypofunction is necessary before the hyperkinetic element of the movement disturbances can manifest itself. 13 references. (Author abstract modified)

000821 Gershon, Samuel. New York University Medical Center, New York, NY **Psychopharmacology of the lithium ion.** Psychopharmacology Bulletin. 12(3):83-84, 1976.

A series of studies is performed to determine: 1) the usefulness of lithium as a preventive for mania; 2) the usefulness of lithium as a prevention for the depressed phase of manic-depression; 3) the effectiveness of lithium as a treatment for schizo/affective illness; 4) the behavioral effects of lithium; 5) the metabolic disposition of the drug; and 6) the interaction of lithium with other exogenous compounds and endogenous compounds. Lithium and haloperidol are superior to chlorpromazine in the treatment of mania. Lithium has a slower onset of action than haloperidol but complete normalization of patients occurs only with lithium. Lithium and iodine have a synergistic effect in producing thyroid disturbance which may result in hypothyroidism, especially in patients who already have an abnormality in thyroid hormone synthesis. Patients ingesting lithium and thyrotropin releasing hormone (TRH) tend to have elevated levels of endogenous thyrotropin. The antithyroid effects of lithium are not due to an effect on the pituitary. Lithium does not appear to possess antidepressant activity in dogs. However, clinical trials have indicated that lithium may be of value in treating acute recurrent depression, especially unipolar depression, in some patients.

000822 Goble, Frans C. Research and Development Division, Cooper Laboratories, Inc., Cedar Knolls, NJ 07927 **Sex as a factor in metabolism, toxicity, and efficacy of pharmacodynamic and chemotherapeutic agents.** Advances in Pharmacology and Chemotherapy. 13:173-252, 1975.

In a continuing series of reports on advances in pharmacology and chemotherapy, the literature on the effect of sex of subject on metabolism, toxicity, and efficacy of pharmacodynamic and chemotherapeutic agents is reviewed in animal and clinical comparisons. Areas covered are: central nervous system depressants and stimulants; psychotropic agents; local anesthetics; and myotropics. Included are: cardiac glycosides; antiinflammatory compounds; antihistamines; hypoglycemic agents; anticoagulants; and diuretics. Also covered are: laxatives; antitussive compounds; antiinfective compounds; and antineoplastic agents. Because other species are not physiologically similar to the rat, most material on the rat has not been included. Instead, other species and findings that have not yet been fitted into a pattern as well worked out have been included. It is suggested that the different responses in the sexes may involve the very fundamental genetic differences resulting from the presence of the two X-chromosomes in the somatic cells of females versus one X-chromosome in those of males. 787 references.

000823 Gottfries, Carl-Gerhard; Oreland, Lars; Wiberg, Asa; Winblad, Bengt. Psykiatriska Kliniken, Lasarettet, S-90185 Umea, Sweden **/Lowered monoamine oxidase in connection with alcoholic suicides./** Sankt monoaminooxidasktivitet hos alkoholister som suicidierat. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):447-451, 1975.

The activity of monoamineoxidase (MAO) in brains of 15 patients who had committed suicide was compared to a control group of 20 brains, which showed no signs of psychiatric or neurological disease. All 35 cases were of the same age. The MAO activity was measured in 13 different parts of each brain with the substrates tryptamine and beta-phenylethylamine. The suicide group showed significantly lower MAO activity in all examined parts compared to the control group with both substrates. In the suicide group were eight alcoholics who had the least MAO activity. Whether this is due to a direct effect of ethanol on the enzyme or that the alcoholic group suffered from affective disturbances is uncertain. The hypothesis of lowered MAO activity in connection with depression is supported by experiments with rat brains where the MAO activity increases after a constant supply of L-Dopa. 15 references.

000824 Hall, R. C.; Brown, Deirdre; Carter, R.; Kendall, M. J. Medical School, Birminghan B15 2TJ, England **The effect of desmethylimipramine on the absorption of alcohol and paracetamol.** Postgraduate Medical Journal (Oxford). 52(605):139-142, 1976.

Many drugs can delay gastric emptying and may already impair the absorption of other drugs. Desmethylimipramine (DMI) is an antidepressant with anticholinergic properties which might be expected to delay the rate of gastric emptying. In five out of six subjects, DMI significantly delayed both the absorption of alcohol (assessed by a breathalyzer) and of paracetamol, and there was a correlation between the two. The breathalyzer can therefore be used to predict the extent to which one may impair the absorption of another drug by its effect on gastrointestinal motility. 10 references. (Author abstract)

000825 Hendel, Jorn. Dept. of Pharmacology, University of Copenhagen, 20 Juliane Mariesvej, DK-2100 Copenhagen, Denmark **Cumulation in cerebrospinal fluid of the N-desmethyl metabolite after long-term treatment with diazepam in man.** Acta Pharmacologica et Toxicologica (Kobenhavn). 37(1):17-22, 1975.

Thirteen patients were given 10mg diazepam (DZ) intramuscularly 12 hrs and 1 hr before spinal puncture. Plasma and cerebrospinal fluid concentrations of DZ and the main metabolite N-desmethyldiazepam (NDDZ) were determined simultaneously in the plasma and the cerebrospinal fluid. Five patients treated with DZ over several months showed a significantly higher NDDZ ratio (cerebrospinal fluid/plasma) than eight patients not previously treated with DZ. This indicates a cumulation of this psychoactive metabolite in the brain of man during long term treatment with DZ. 15 references. (Author abstract modified)

000826 Johnsson, Gillis. Department of Medicine II, Sahlgrenska Hospital, S-413 45 Goteborg, Sweden **Influence of metoprolol and propranolol on hemodynamic effects induced by adrenaline and physical work.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):59-68, 1975.

The influence of intravenously administered metoprolol, propranolol, and saline on hemodynamic effects induced by adrenaline and physical work were studied in healthy volunteers. The two beta-blockers were approximately equipotent in reducing the heart rate and systolic blood pressure in the doses used during exercise, and they interacted differently with adrenaline. When adrenaline was infused after propranolol, the mean and diastolic blood pressure increased as did vascular resistance in the forearm. Adrenaline had no significant effect on the forearm blood flow, while the heart rate decreased. The difference in interaction of the two beta-blockers with adrenaline is interpreted as being caused by a much less pronounced effect of metoprolol on the adrenergic vascular beta2-receptors compared to propranolol in the doses studied. 11 references. (Author abstract modified)

000827 Johnsson, Gillis; Nyberg, Gunnar; Solvell, Lennart. Research Laboratories, AB Hassle, Fack, S-431 20 Molndal, Sweden **Influence of metoprolol and propranolol on hemodynamic effects induced by physical work and isoprenaline.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):69-75, 1975.

The effects of metoprolol (40mg and 80mg orally as hydrochloride) and propranolol (40mg orally as hydrochloride) were compared on the increase of heart rate and systolic blood pressure induced by physical exercise and infusion of isoprenaline in healthy volunteers. The two beta-blockers seemed to be equipotent in reducing heart rate and systolic blood pressure during exercise, while they differed considerably in their interaction with isoprenaline. Thus, the isoprenaline induced increase of the heart rate was blocked to a considerably greater extent after propranolol than after metoprolol. The reason for this is discussed and can be explained by the selectivity of metoprolol for beta1-receptors. 10 references. (Author abstract modified)

000828 Johnsson, Gillis; Regardh, Carl-Gunnar; Solvell, Lennart. Research Laboratories, AB Hassle, Fack, S-431 20 Molndal, Sweden **Combined pharmacokinetic and pharmacodynamic studies in man of the adrenergic beta1-receptor antagonist metoprolol.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):31-44, 1975.

The adrenergic beta1-receptor antagonist metoprolol was given orally and intravenously in varying doses to five healthy volunteers. Effect on heart rate during exercise was linearly related to the logarithm of the dose and the plasma concentration. The most pronounced effect was obtained during the first exercise test after administration (one hour after oral and 20 minutes after intravenous administration). The effect declined linearly with time (zero order kinetics) and at virtually the same rate for all doses investigated. The time for 50% reduction of the maximally registered effect was 6.4hours after 100mg metoprolol orally and 5.0hours after 50mg. The plasma concentration of metoprolol declined monoexponentially with time at a rate corresponding to an elimation half-life of about three hours. The relationship between the areas under the plasma concentration curves after oral and intravenous administration indicated a bioavailability of 40% to 50% for the two highest oral doses. In accordance with this the ratio between equipotent oral and intravenous doses was about 2.5. 18 references. (Author abstract modified)

000829 Jorgensen, Aksel. Biochemical Dept., H. Lundbeck & Co., A/S, 7-9 Ottiliavej, DK-2500 Copenhagen, Denmark **A gas chromatographic method for the determination of amitriptyline and nortriptyline in human serum.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(1):79-90, 1975.

Amitriptyline (AMT) and nortriptyline (NT) were extracted from human serum with hexane at pH 9. An internal standard was added and extracted with the drugs. During the concentration of the hexane phase nortriptyline was acetylated to improve separation. One fifth of the final hexane phase was injected into a gas chromatograph equipped with a detector, which was selectively sensitive towards nitrogen. The lower limits of detection were 5ng/ml for AMT and 10-15ng/ml for NT. A constant relative standard deviation of 7.6% was found in the concentration interval used for the standard curves. No interference appeared from AMT metabolites and some benzoediazepines. The method has been used for the estimation of AMT after a single dose of this drug to two human volunteers and for the estimation of AMT and NT after repeated administration of amitriptyline to patients. After single dose administration NT was not detectable, while the NT concentration was of the same order as the AMT concentration after repeated administration. A great individual variation in the concentrations of the two drugs was seen after repeated administration. 10 references. (Author abstract)

000830 Jovanovic, U. J. Universitats-Nervenklinik u Poliklinik, Wurzburg, Germany **Statistical evaluation of polygraphic investigations of pentoxifylline.** Journal of International Medical Research (Northampton). 4(4):211-222, 1976.

Changes in the electroencephalogram, and in the electrooculogram electromyogram, ECG, blood supply, blood pressure, electrical skin activity and neurological/psychiatric findings, were investigated in 100 patients given single administrations of 200mg of pentoxifylline (BL 191). It is concluded from the changes in the EEG wave patterns that pentoxifylline produces a beneficial effect on the cerebral processes contributing to bioelectrical brain activity. Pentoxifylline can be classed as a substance with microcirculatory/metabolic effects on the brain, which lead to simulation of psychomotor behavior. 15 references. (Journal abstract)

000831 Kanabus, Piotr. Zaklad Analityki Klinicznej, Instytut Biofarmacji, AM, ul. Banacha 1, 02-097 Warszawa, Poland **/Current views on the mechanism of chlorpromazine action./** Aktualne poglady na temat mechanizmu dzialania chloropromazyny. Psychiatria Polska (Warszawa). 10(2):189-195, 1976.

Current views on the mechanism of action of chlorpromazine (CPZ) are generally summarized. The fact that only 1% of the drug may be detected in its original form in the urine, the large number of metabolites that are formed, and the low level of CPZ typically found the bloodstream even shortly after administration cause many analytical difficulties. Although used extensively and effectively in the treatment of schizophrenia, problems are caused by the fact that only a certain optimum blood level of CPZ produces signs of improvement, and the dosage necessary for this varies from patient to patient. It is believed that further research will establish the complete mechanism of action, the optimum dosage, and side-effects of CPZ. 31 references.

000832 Kanto, J.; Kangas, L.; Siirtola, T. Dept. of Pharmacology, Univ. of Turku, Kiinamyllynk.10, Turku 52, Finland **Cerebrospinal-fluid concentrations of diazepam and its metabolites in man.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(4):328-334, 1975.

Plasma and cerebrospinal fluid (CSF) concentrations of diazepam, its main metabolite, N-demethyldiazepam, and free oxazepam were studied gas chromatographically in 49 patients suffering from neurological diseases, after a 10mg intramuscu-

lar dose of diazepam. These determinations were made in three other patients after repeated intramuscular doses of 10mg diazepam. In seven of the patients both free and plasma protein bound diazepam, and N-demethyldiazepam were determined by ultracentrifugation after a single dose of 10mg intramuscular diazepam. After a single dose of diazepam there was only 2%-3% of the total plasma concentration of diazepam and 1%-4% of that of N-demethyldiazepam in the CSF. After repeated doses of diazepam the same values were 3% and 4% respectively. The plasma protein binding capacity of diazepam was 98% and that of N-demethyldiazepam 97%. Free diazepam and N-demethyldiazepam concentrations in the plasma were in equilibrium with their CSF concentrations. No accumulation of diazepam and N-demethyldiazepam could be found in the CSF. No free oxazepam was found. 21 references. (Author abstract)

000833 Keul, J.; Huber, G.; Kindermann, W.; Burmeister, P.; Petersen, K. G. Medizinische Univ. - Klinik, Hugstetter Strasse 55, BRD-7800 Freiburg, West Germany **/Effect of new beta-adrenergic receptor blocking agent (Bunitrolol) on circulation and metabolism under conditions of extreme stress./** Die Wirkung eines neuartigen Beta-Rezeptorenblockers (Bunitrolol) auf Kreislauf und Stoffwechsel unter extremen Stressbedingungen. Medizinische Welt (Stuttgart). 27(9):437-443, 1976.

The effect of the new beta-adrenergic receptor blocking agent Bunitrolol on circulation, metabolism and performance of men acting under conditions of extreme psychological stress was studied. Twelve team bobsledders with a mean age of 27, including world masters and Olympic medalists, were studied before, during and after four races. Bobsledders were chosen because of the extreme mental tension and danger they face and the reproductible nature of emotional stress conditions encountered on the bobsled course. On 2 days the bobsledders were given either 20mg Bunitrolol or a placebo approximately 90 min, before the test. In races under the influence of the placebo heartbeats averaged 170-180/min, with individual cases exceeding 200/min. After taking Bunitrolol (p.o.)this excessive increase in heart rate was reduced by an average value of 40-50 heartbeats per minute. The increase of free fatty acids and glycerol in the blood serum due to increased lipolysis was no longer observed after Bunitrolol. The drug did not affect the glucose, triglyceride, glycerine, cholesterol, somatotropic hormone, or insulin levels. There was a smaller increase in the lactate level, and a consequentially smaller decrease in the alkaline excess and pH values. The stress conditioned excessive reaction of the heart and metabolism is dampened by Bunitrolol. In bobsledding the drug improved driving abilities and the bobsledders felt subjectively more capable of performing after taking the drug. 55 references.

000834 Kittner, Steven; Lipsitt, Lewis P. Dept. of Psychology, Brown University, Providence, RI 02912 **Obstetric history and the heart-rate response of newborns to sound.** Developmental Medicine and Child Neurology (London). 18(4):460-470, 1976.

The relationship between obstetric history and newborn behavior was examined, comparing two groups of clinically normal newborns, differing in the number of nonoptimal factors in their obstetric history, by measuring heartrate response to a series of auditory stimuli. There was a significant difference between the groups in the direction of the average heartrate response. The high risk group showed more heartrate acceleration and less deceleration compared with the low-risk group. The heartrate responses were significantly related to the number of nonoptimal obstetric conditions and to parity, but not to the maternal predelivery medication score. The greater the risk at birth, the less was the deceleration. The greater the maternal parity, the less did acceleration occur in response to auditory stimulation. There was no significant difference between the high-risk and low-risk groups in heartrate response trends over trials. Both groups showed reliable diminution of deceleration heartrate response over trials. 36 references. (Author abstract)

000835 Korttila, K.; Mattila, M. J.; Linnoila, M. Dept. of Pharmacology, Univ. of Helsinki, Siltavuorenpenger 10 A, SF-00170 Helsinki 17, Finland **Saturation of tissues with N-desmethyldiazepam as a cause for elevated serum levels of this metabolite after repeated administration of diazepam.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(2):190-192, 1976.

It is demonstrated that elevated serum levels of N-desmethyldiazepam after repeated administration of diazepam may be due to saturation of tissues with N-desmethyldiazepam rather than to diazepam inducing its own metabolism. 5 references.

000836 Korttila, K.; Sothman, A.; Andersson, P. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Polyethylene glycol as a solvent for diazepam: bioavailability and clinical effects after intramuscular administration, comparison of oral, intramuscular and rectal administration, and precipitation from intravenous solutions.** Acta Pharmacologica et Toxicologica (Kobenhavn). 39(1):104-117, 1976.

The bioavailability of diazepam (10mg) was compared in a double-blind crossover manner in two studies on 15 healthy subjects. Serum diazepam levels were measured and the occurrence of pain at the injection site as well as fatigue was noted 20, 40, 60, 90 and 180 min after the administration of 0.15mg/kg of diazepam to seven subjects. Three intramuscular preparations were used: valium (Roche), diapam (Orion) and 301 K 2/74 (Orion). The last mentioned preparation contained only half the propylene glycol contained in the other preparations, and polyethylene glycol (Macrogol) was the main solvent. The other eight subjects were similarly tested after the administration of diazepam orally, intramuscularly and rectally. In addition the precipitation of diazepam from intravenous solutions was investigated with diazepam in both solvents. Bioavailability and fatigue are similar after each treatment. 301-K 2/74 and its solvent placebo caused significantly less pain in the thigh than valium or diapam. The results suggest that an intramuscular injection of diazepam into vastus lateralis muscle, and rectal and oral administration result in comparable bioavailability and clinical effects. A reduction in the amount of propylene glycol solvent used is associated with less pain at the injection site. When diapam is injected into an infusion tube at a rate of 5mg/min, the rate of infusion of 5% glucose or 0.9% saline must be as fast as 20ml/min in order to prevent visible precipitation, whereas no precipitation is observed when 301-K 2/74 is injected at the 5mg/min rate into infusions moving at 5ml/min. Further clinical studies with intramusular and intravenous 301-K 2/74 are warranted. 25 references. (Author abstract modified)

000837 Lader, M. Dept. of Clinical Psychopharmacology, Institute of Psychiatry, University of London, London, England **Monitoring plasma concentrations of neuroleptics.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(4):170-177, 1976.

The literature dealing with the pharmacokinetics of chlorpromazine is reviewed and the results evaluated and discussed. Chlorpromazine has been the most extensively studied neuroleptic despite its complex metabolic pathways. Several metabolites, in particular 7-hydroxychlorpromazine, are psychotropically active. Oral phenothiazines are extensively metabolized through the liver. The relationship between clinical response and plasma concentrations of neuroleptics is tenuous. The reasons for the lack of correlation include spontaneous remission in some patients, problems with flexible dosage schedules, the type of patient studied, differences in metabolic patterns, induction of metabolism in the liver, interactions with other drugs, and variations in plasma protein binding. Alternative research strategies might be to study metabolically less complex drugs such as haloperidol or to relate clinical response to autonomic, extrapyramidal, EEG, biochemical or endocrine measures. 39 references. (Author abstract modified)

000838 Leonhardt, Klaus-Frithjof. Neurologische Klinik der Universitat Hamburg, Martinistrasse 52, Hamburg-Eppendorf 2, Germany **/Schizophrenia and neuroendocrine functional disorder: a case study on the problem of paranoid psychosis./** Schizophrenie und neuro-endokrine Funktionsstorung -- eine Fallstudie zum Problem der paranoiden Psychose. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 27(10):584-591, 1975.

The case of a 37-year-old female patient suffering from paranoid schizophrenia plus a neuroendocrine disorder is reported, and a possible causal relationship between neuroendocrine dysfunction and the multifactorial genesis of schizophrenia is discussed. Schizophrenia research has shown remarkable agreement on the subject of ascribing the etiology of schizophrenia to the limbic system, including structures of the hypothalamus, N. amygdalae, hippocampus, fornix, gyrus cinguli and the frontal occipital brain. According to studies by Fuxe and others (1970), endocrine maturational and functional disorders are due to pathologies of the limbic, extrapyramidal/motor and hypothalamic/hypophyseal neuroendocrine system, which can also cause psychological disorders. Correlation of evidence from the field of psychopharamcology includes a discovery by Borenstein et al. of a psychotropic drug, a sulpiride/pyrrolidinyl/benzamide derivative, that has endocrinologic, but not the anticipated extrapyramidal side-effects. 20 references.

000839 Lewis, Stuart A. Department of Psychiatry, University of Nottingham Medical School, Mapperley Hospital, Nottingham, England **Benzodiazepines and human sleep.** Bulletin of the British Psychological Society (London). 28:241, 1975.

The role of benzodiazepines in producing human sleep is examined, emphasizing that although these drugs have many advantages over barbiturates such as clinical safety, there is little difference when the internal structure of sleep is considered. Both classes of hypnotic will reduce paradoxical sleep and slow wave sleep as well as reducing restlessness. Withdrawal of the drugs leads to CNS disturbances apparent during sleep. Observation of endocrine function during sleep indicates that it, too, is altered by the drugs, and these findings may help explain some clinical observations. While the function of sleep is unknown, the effects of the drugs may be thought of in terms of alterations in the synthetic processes of growth and renewal and the body's attempt at restoration of homeostatic balance. (Author abstract)

000840 Linnoila, M.; Korttila, K.; Mattila, M. J. Dept. of Pharmacology, Univ. of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 10, Finland **Effect of food and repeated injections on serum diazepam levels.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(2):181-186, 1976.

To determine effects in combination with foods, diazepam 0.3mg/kg was administered intravenously three times at intervals of 14 days into seven healthy volunteers. Five hours after injection the subjects ingested either 330ml of mineral water, mineral water in combination with 2 rusks, or 330ml of fatty milk with an egg hamburger. Diazepam and N-desmethyldiazepam levels were measured in serum samples drawn at 4, 5, 6, 7 and 8 hours after administration of the drug. At the same time the ability to discriminate flickering light was measured, and the feeling of tiredness was recorded. The serum diazepam levels declined regularly as function of time after mineral water, but both kinds of food significantly elevated the serum diazepam level from the sixth hour onwards. The ability to discriminate flickering light was not modified. Serum N-desmethyldiazepam levels were significantly elevated after the second and third injections as compared with the first injection. Serum diazepam levels were not lowered. The present findings could be explained by an enterohepatic cycle of diazepam, and suggest that diazepam might induce its own metabolism in man. 8 references. (Author abstract)

000841 Lovstad, Rolf A. Institute of Medical Biochemistry, University of Oslo, Karl Johans gt 47 Oslo 1, Norway **Interaction of some neuroleptic and antidepressive agents with human coeruloplasmin.** Biochemical Pharmacology (Oxford). 25(16):1877-1879, 1976.

Human coeruloplasmin oxidase activity towards several neuroleptic drugs and antidepressant drugs was investigated. Prothipendyl, an azaphenothiazine, had the same Vmax value as its phenothiazine analog promazine. At lower substrate concentrations prothipendyl was more slowly oxidized that promizine. Imipramine, desipramine, and opipramol were more slowly oxidized by coeruloplasmin than promazine, while chlorprothixene, tiothixene, amitriptyline, portriptyline, and haloperidol did not react at all. It is suggested that a central ring nitrogen atom is essential for oxidase activity. The folded phenothiazine ring system is favorable for a rapid reaction. The best substrates, promazine and prothipendyl, activated the coversion of noradrenaline to noradrenochrome in the presence of coeruloplasmin. 21 references. (Author abstract modified)

000842 Mandell, Arnold J.; Segal, David S.; Kuczenski, Ronald. Department of Psychiatry, School of Medicine, University of California, San Diego, La Jolla, CA **Metabolic adaptation to antidepressant drugs: implications for pathophysiology and treatment in psychiatry.** In: Friedhoff, A., Catecholamines and behavior. Vol. 2. New York, Plenum Press, 1975. 225 p. (p. 197-208).

The five macromolecular mechanisms involved in the regulation of neurotransmitter synthesis and efficacy in central synaptic systems are reviewed. The long-term changes in tyrosine hydroxylase following chronic administration of the antidepressant drugs, reserpine and desmethylimipramine are discussed, and these changes are related to chronic unit discharge activity in biogenic amine neurons and discussed in relation to a biochemical model of depression as pathological activation. The model postulates that the reduction in presynaptic nerve firing rate results from feedback following the facilitation of transmission when reuptake of amine is blocked by a drug, and that this decreased firing rate results in

the decrease in the synthesis and flow of tyrosine hydroxylase to the nerve ending. A revised theory of depressive illness is presented, suggesting that the efficacy of tricyclic antidepressants in a group of unipolar depressive patients, who reveal in their red blood cells primary or secondary deficiency of catachol-o-methyltransferase, indicates a syndrome of hyperactive central biogenic amine systems. The tricyclics quiet the agitation by prompting the lagging compensatory mechanisms to further decrease the neuronal firing rate and, consequently, the enzymatic capacity to synthesize neurotransmitters, thereby protecting the receptors. 26 references.

000843 Massari, Vito John. Vanderbilt University, Memphis, TN **Central mechanisms of action of p-chloroamphetamine: biochemical and histological studies. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-15495 HC$15.00 MF$8.00 194 p.

The effects of 10mg/kg of p-chloroamphetamine (PCA) on serotonergic axons in the central nervous system were observed on 1, 2, 4, 6, and 14 days. No degeneration was observed, and it is concluded that PCA probably does not cause the degeneration of serotonergic axons in the central nervous system. A comparison of the biochemical effects of lesions of the B-9 cell group with those caused by PCA indicates that the biochemical effects of PCA could not be due to a selective cytotoxic effect on B-9 cells, as has been recently suggested. In addition, the evidence indicated that a lateral serotonergic pathway, possibly from the B-9 cell group, projects to the metathalamus/thalamus. Arguments were marshalled that PCA is not toxic to most serotonergic cell bodies, i.e. those of the dorsal and median raphe nuclei. Since the evidence indicates that PCA is also not toxic to serotonergic cell axons, it is concluded that neurotoxic characteristics of PCA may be due to a selective degeneration of serotonergic nerve terminals. (Journal abstract modified)

000844 Matussek, N. Psychiatr. Klinik der Univ., Nussbaumstrasse 7, 8000 Munich 2, West Germany **/Theoretical basis of therapy with neuroleptics and antidepressants./** Theoretische Grundlagen der Therapie mit Neuroleptika und Antidepressiva. Medizinische Welt (Stuttgart). 27(11):508-511, 1976.

The general effects of neuroleptics and antidepressants on the metabolism of the CNS are described to familiarize general practitioners with the theoretical basis for therapy with psychotropic drugs. All neuroleptics currently known influence dopamine metabolism in the CNS by blocking dopamine receptors. All classic antidepressants, including the newly developed types with different chemical structures, influence the metabolism of serotonin. Mianserin increases the production of catecholamine through a still unexplained mechanism. The metabolism of different antidepressants varies considerably and dosage cannot be routinely set. Low dosage of tricyclics is ineffective, and even the recommended dosage may fail to give the desired therapeutic effect in some patients and is reflected by low plasma concentrations. High dosages are equally ineffective because they may block the postsynaptic receptors. 10 references.

000845 Melzack, Ronald; Ofiesh, J. G.; Mount, Balfour M. Department of Psychology, McGill University, P.O. Box 6070, Station A, Montreal, PQ H3C 3G1, Canada **The Brompton mixture: effects on pain in cancer patients.** Canadian Medical Association Journal. 115(2):125-129, 1976.

Terminally ill cancer patients were given the Brompton mixture and a phenothiazine in an attempt to control their pain: the mixture was administered to patients in three hospital environments (a Palliative Care Unit (PCU), a general ward, and private rooms) and pain was measured in 92 patients with the McGill Melzack Pain Questionnaire. The Brompton mixture controlled pain in 90% of patients in the PCU and in 75% to 80% of patients in the wards or private rooms. The differences in pain scores between the PCU patients and the other groups ere significant. The mixture produced substantial decreases in the three major dimensions of pain: sensory, affective and evaluative. Comparison of these results with data obtained in an outpatient clinic showed that the Brompton mixture was strikingly more effective than he traditional methods of managing cancer pain. 10 references. (Author abstract)

000846 Mendelson, Wallace B.; Goodwin, Donald W.; Hill, Shirley Y.; Reichman, John D. NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Hypnotics and ethanol: residual EEG effects.** Bethesda, MD, NIMH, 1976. 1 p.

The possible synergistic interaction of ethanol and benzodiazepines was examined by recording 12 min waking clinical electroencephalographs (EEGs) of normal young men who received 0.24mg triazolam, 30mg flurazepam, or placebo, alone or in combination with 0.8g/kg ethanol. EEGs were performed as a baseline 50 min after drug administration, 50 min after ethanol administration, and 16 hrs after having received the drug. Findings suggest that ethanol produces a small, but significant, increase in the duration of EEG effects of flurazepam. Flurazepam along is known to remain active for some time. Thus, repeated use of the drug might produce cumulative effects, which may possibly be increased by ethanol. 5 references.

000847 Mount, Balfour M.; Ajemian, I.; Scott, J. F. Palliative Care Service, Royal Victoria Hospital, 687 Pine Avenue West, Montreal, PQ H3A 1A1, Canada **Use of the Brompton mixture in treating the chronic pain of malignant disease.** Canadian Medical Association Journal. 115(2):122-124, 1976.

Three case histories illustrate the use of the Brompton mixture (a highly effective, flexible, safe and convenient means of controlling the chronic pain of malignant disease) for periods ranging from 9 weeks to more than 1 year. The Brompton mixture is a solution containing morphine; the dose of narcotic can be varied with the need for analgesia. It is given regularly, usually every 4 hours, with a phenothiazine, the main aims of therapy being prevention of pain rather than treatment, an unclouded sensorium and a normal affect. Eight factors which are important in adjusting the dosage of medication to achieve a pain free state without sedation are noted. Adversive effects, which are basically those common to all narcotics, are discussed. 13 references. (Author abstract modified)

000848 Nardini, M.; Sciannandrone, R.; Fieschi, C.; De Simone, G. Clinica delle Malattie Nervose e Mentali, Universita di Siena, Siena, Italy **/Piribedil in the treatment of Parkinson's disease./** Ruolo del piribedil nel trattamento del morbo di Parkinson. Rivista di Patologia Nervosa e Mentale (Firenze). 96(2):103-110, 1975.

Because of the clinically demonstrated effectiveness of apomorphine in the treatment of Parkinson's disease, a laboratory hypothesis that piribedil, a drug resembling apomorphine, should be effective against Parkinson's disease was tested. A group of 17 patients, nine males and eight females, 53 to 70 years of age, with either Parkinson's disease or postencephalitic parkinsonism, was subdivided and treated with piribedil under single-blind conditions for periods of 5 weeks to 24 months. Analysis of the results showed piribedil modified extrapyramidal symptomatology, and was particularly

effective against tremor either when used alone or in association with L-dopa. Side-effects noted were similar to those of apomorphine and were dose dependent. 10 references. (Author abstract modified)

000849 Naylor, G. J.; Dick, D. A. T.; Dick, E. G. Department of Psychiatry, University of Dundee, Scotland **Erythrocyte membrane cation carrier, relapse rate of manic-depressive illness and response to lithium.** Psychological Medicine (London). 6(2):257-263, 1976.

Measures of the erythrocyte membrane cation carrier are correlated with clinical events, remote in time from the biochemical assay. Erythrocyte sodium concentration, ouabain sensitive potassium influx and Na-K ATPase were estimated in 11 patients with the diagnosis of manic-depressive psychosis before and after the crossover point in a two year double-blind ATPase and the highest flux sodium ATPase ratio tended to suffer most episodes of affective illness in the two years. Patients who had a low initial Na-K ATPase or a high initial flux sodium ATPase ratio, or in whom the ratio fell most with lithium, or whose Na-K ATPase rose most with lithium, clinically responded best to lithium. 22 references. (Journal abstract modified)

000850 Niazi, Sarfaraz. Department of Pharmacy, College of Pharmacy, University of Illinois at the Medical Center, Chicago, IL 60612 **Comparison of observed and predicted first-pass metabolism of imipramine in humans.** Journal of Pharmaceutical Sciences. 65(7):1063-1064, 1976.

The first pass metabolism of imipramine was calculated based on the dose, hepatic blood flow and total area under the plasma/time curve after oral administration of 0.71mg/kg of imipramine to four mildly depressed patients. The average determined value is 52.75%. The predicted value calculated using the equation proposed by Gibaldi and coworkers (1971 and 1975) is 58.25%. It is suggested that the predicted value obtained via the equation correlates very well with the experimentally determined value. 3 references. (Author abstract modified)

000851 Numata, Yoshihiko; Hoshino, Kunihiko; Kobayashi, Yukio; Koizumi, Shinsuke; Umio, Yukihiro; Kaneko, Motohisa. Department of Neuropsychiatry, Iwate School of Medicine, Iwate Prefecture, Japan **The effect of oxypertine on tardive dyskinesia.** Psychiatria et Neurologia Japonica (Tokyo). 77(7):523, 1975.

The drug oxypertine was used on fifteen patients afflicted with Tardive Dyskinesia to test its effect. The drug was administered over a period of 1 to 13 months (the average was 4 months). The dosage varied between 20 and 120mg daily, but the overall average was 80mg. Results observed were marked improvement in two cases, 50mg improvement in seven cases, slightly effective in three and not effective in three other cases. The overall effectiveness rating was 60%. Blood serum tests were also performed to determine indoleamine in Tardive Dyskinesia, but no significant relationship was found. Comparative tests of oxypertine against other anti-Parkinsonian drugs were not made.

000852 Patrizi, C.; Pennelli, G.; Romano, D.; Scoppola, L. no address **/Psychosomatosis with common cardiac localization: experiences with sulpiride in internal medicine./** Le psicosomatosi a prevalente localizzazione cardiaca: esperienze condotte con il sulpiride in medicina interna. Medicina Psicosomatica (Roma). 20(4):430, 1975.

A study of the use of sulpiride in internal medicine patients with vascular and cardiac disorders was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Because the physician is not usually in a position to evaluate all psychosomatic problems a patient has, it was suggested that the patient evaluate his own emotional situation while being treated with sulpiride. Such treatment has had good therapeutic effects with hospitalized patients.

000853 Pelton, E. Williams, II; Chase, Thomas N. Laboratory of Clinical Science, NIMH, Bethesda, MD **L-dopa and the treatment of extrapyramidal disease.** Advances in Pharmacology and Chemotherapy. 13:253-304, 1975.

In a continuing series of reports on advances in pharmacology and chemotherapy, the literature on L-dopa and the treatment of extrapyramidal disease is reviewed. The principal focus of the review is on the function of central dopamine containing neural systems in view of their crucial role in mediating the effects of L-dopa on motor behavior. The areas covered are: metabolism; pharmacology; and therapeutic applications. The fortuitous circumstances which contribute to the ability of L-dopa to improve Parkinsonian signs are discussed. 351 references.

000854 Petersen, B. H.; Graham, J.; Lemberger, L. Lilly Laboratory for Critical Research, Indianapolis, IN 46202 **Marihuana, tetrahydrocannabinol and T-cell function.** Life Sciences (Oxford). 19(3):395-400, 1976.

Chronic marihuana smokers, who had abstained from smoking for 1 month, smoked "street" marihuana, marihuana cigarettes with a known quantity of delta9-tetrahydrocannabinol or placebo marihuana cigarettes in a study designed to determine what, if any, relationship existed between the time of sampling and any alterations in T-lymphocyte (T-cell) responsiveness. The results support the conclusion that while marihuana smoking does affect T-cell function, these effects are transitory, vary significantly from subject to subject, and are closely related to the time at which the samples were obtained. It appears that the response to mitogenic stimulation can be affected in some individuals and that the circumstances of testing could give rise to the conflicting results currently in the literature. 19 references. (Author abstract modified)

000855 Pollock, Steven Hayden. Dept. of Pharmacology, University of Texas Health Science Center, San Antonio, TX 78284 **Psilocybian mycetismus with special reference to Panaeolus.** Journal of Psychedelic Drugs. 8(1):43-57, 1976.

Intoxication experiences from a literature review of all Paneolus species, and the cultural/religious patterns of use are documented. The psilocin and psilocybin synthesizing capabilities of numerous Paneolus are reviewed and compared to Copelandia and Psilocybe species. The bluing phenomenon of P. subbalteatus considered causative of cerebral mycetisms and potentially hallucinogenic is discussed in a review of in vivo and in vitro animal studies. Paneolus and other psilocybian mushrooms are highly recommended for altering states of consciousness in psychotherapy and preferred to LSD or mescaline because of shorter acting effects, fewer adverse reactions, fewer flashbacks, and less postsession depression. 127 references.

000856 Pozenel, H.; Bueckert, A.; Amrein, R. no address **Further hemodynamic investigations of the antihypertensive effect of "Lexotan" (bromazepam).** Medicina Psicosomatica (Roma). 20(4):420-421, 1975.

Results of hemodynamic investigations of the antihypertensive effect of Lexotan were discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Lexotan is believed to exhibit a antihypertensive effect in patients suffering from grade 1 and grade 2 essential hypertension. Hemodynamic changes were observed in 15 grade 1 and grade 2 hypertensive patients after I V administration of 1mg and 4mg bromazepam per kg bodyweight. A striking reduction in mean pressure was effected by a fall in both systolic and diastolic pressure. The hypotensive effect was largely due to a 17% reduction in total peripheral resistance. The cardiac index was not significantly decreased, and heart rate was only slightly reduced. Diastolic and systolic pressure in the pulmonary artery were unchanged. There was no mentabolic alteration in values of blood gases. The solvent, injected under identical conditions, caused no hemodynamic changes, no fall in blood pressure, insignificant change in heart rate, and no reduction in peripheral resistance. other circulatory features were also unaffected. Various explanations for the antihypertensive effect of bromazepam were discussed. (Author abstract modified)

000857 Raaflaub, J. no address **The pharmacokinetics of bromazepam in man.** Medicina Psicosomatica (Roma). 20(4):421, 1975.

A report on the pharmacokinetics of bromazepam in man was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). The absorption, distribution, and elimination characteristics of a single oral dose of bromazepam in man were discussed. Similarities and differences of the pharmacokinetic profile of bromazepam compared with the profile of diazepam were outlined and discussed. In addition, data on the plasma levels were found and those calculated for chronic oral treatment with the drug were reported. (Author abstract modified)

000858 Randrup, A.; Munkvad, I.; Fog, R.; Ayhan, I. H. Research Laboratory, Department E., Hans Hospital, Roskilde, Denmark **Catecholamines in activation, stereotypy, and level of mood.** In: Friedhoff, A., Catecholamines and behavior. Vol. 1. New York, Plenum Press, 1975. 235 p. (p. 89-107).

The association of catecholaminergic systems in the brain with behavioral activation, level of mood and stereotypy is explored. Observation of drug effects in animals has been the principle source of knowledge of this association. The amphetamine induced behavioral activation and stereotypy is hypothesized as being due to overactivity of dopaminergic brain systems. The morphine induced behavioral activation and stereotypy is associated with increased noradrenergic activity in the brain. Pharmacological data on drug action in the human system, although not conclusive because the drugs are never completely specific to one of several brain systems, add insight to the role of brain dopamine in schizophrenia, mania, abortive thinking, psychoses and depression. Pharmacological and biochemical evidence of the effects of amphetamines and neuroleptics is discussed, drawn from clinical observations of patients afflicted with these disorders. 128 references.

000859 Regardh, Carl-Gunnar; Johnsson, Gillis; Jordo, Lars; Solvell, Lennart. Research Laboratories, AB Hassle, Fack, S-431 20 Molndal, Sweden **Comparative bioavailability and effect studies on metoprolol administered as ordinary and slow-release tablets in single and multiple doses.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):45-48, 1975.

The bioavailability, plasma levels and pharmacological effects of 100mg of metoprolol tartrate administered as an ordinary and as 2 different slow release (SR) preparations were compared in healthy volunteers after single and multiple doses in one experiment. In another the urinary excretion of metoprolol and total radioactivity during 72 hours were determined after single doses of 50mg of metoprolol-(3H) tartrate in solution and in 2 SR tablets with different dissolution rates. Administration of metoprolol in SR form reduced peak plasma levels, delayed the time to reach the peak in comparison with the ordinary tablet, and did not significantly influence urinary recovery or the fraction of the radioactive dose excreted by the kidney. Effect variables and plasma levels on heart rate and systolic blood pressure are reported. 9 references. (Author abstract modified)

000860 Reidenberg, Marcus M.; Lowenthal, David T.; Briggs, William; Gasparo, Maryanne. Department of Pharmacology, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Pentobarbital elimination in patients with poor renal function.** Clinical Pharmacology and Therapeutics. 20(1):67-71, 1976.

The mixed function oxidase system in uremic patients was studied using pentobarbital as the test drug. Eleven normal subjects and nine uremic patients were given 100mg of pentobarbital orally. Several blood samples were drawn over a 36 hr period starting on the morning after the dose. Plasma pentobarbital concentration was measured by GLC. The log concentration values were graphed against time elapsed after dose for each patient, and plasma half-life and extrapolated value of concentration at the time of drug administration were determined. The half-life values in normal subjects range from 18 hr to 48 hr (mean 26.5hr). In uremic patients half-life values are 10 hr to 38 hr (mean 21.3hr). In four of the uremic patients, half-life values are below the lowest values obtainable in normal subjects. The apparent volumes of distribution of pentobarbital were 62 L in the normal subjects and 58 L in the uremic patients. Uremeic patients with short half-life values tend to have small apparent volumes of distribution so that the metabolic clearance rates are normal. It is concluded that pentobarbital elimination is normal in patients with renal failure. Some uremic patients have short plasma half-life values for pentobarbital, and these more likely result from low apparent volumes of distribution with normal metabolism clearance rates than from accelerated metabolism of pentobarbital. 32 references. (Author abstract modified)

000861 Rivera-Calimlim, Leonor; Nasrallah, Henry; Strauss, John; Lasagna, Louis. University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **Clincical response and plasma levels: effect of dose, dosage schedules, and drug interactions on plasma chlorpromazine levels.** American Journal of Psychiatry. 133(6):646-652, 1976.

Plasma chlorpromazine (CPZ) levels of 50 psychotic inpatients were measured by gas liquid chromatography; the clinical progress of 29 of these patients with acute psychoses was also assessed. CPZ levels of 50 to 300mg/ml were usually associated with clinical improvement; there was also a relationship between CPZ levels and increases in certain symptoms. Trihexyphenidyl decreased plasma CPZ in 12 of 15 patients. A single 400 to 800mg dose of CPZ at bedtime produced steady states equal to or better than those achieved with multiple doses. Those patients who failed to attain CPZ levels of more than 70mg/ml despite doses of 400 to 1000mg/day were receiving lithium throughout the study and had discharge diagnoses of manic-depressive psychosis, manic type, and schizoaffective schizophrenia. 21 references. (Author abstract modified)

000862 Sellman, R.; Kanto, J.; Pekkarinen, J. Dept. of Pharmacology, Univ. of Turku, Kiinanmyllynk. 10, Turku 52, Finland **Biliary excretion of diazepam and its metabolites in man.** Acta Pharmacologica et Toxicologica (Kobenhavn). 37(3):242-249, 1975.

Ten mg diazepam was given intravenously to 12 patients with a T-tube in the common bile duct after choledochotomy (Group 1) and to 10 patients after cholecystectomy (Group 2). The concentrations of diazepam, of its main metabolite, N-demethyldiazepam, and of free oxazepam in the plasma of both groups and the conjugated and free concentrations of diazepam, N-demethyldiazepam, and oxazepam in the bile in Group 1 were measured by gas chromatography. In Group 1 significantly lower plasma diazepam concentrations were obtained as compared with Group 2 indicating an enterohepatic circulation of diazepam. There was no significant difference in the concentrations of N-demethyldiazepam in the plasma between the two groups. In Group 1 the patients had frequently more free oxazepam in their plasma than in Group 2. The main conjugated metabolite in the bile was N-demethyldiazepam (about 74%). Traces of diazepam were in the conjugated form, but no conjugated oxazepam was found in the human bile. The enterohepatic circulation of diazepam and its metabolites may be partly responsible for the prolonged effects of diazepam. 25 references. (Author abstract)

000863 Sellman, R.; Kanto, J.; Raijola, E.; Pekkarinen, A. Psychiatric Clinic, Turku Municipal Hospital, Turku, Finland **Human and animal study on elimination from plasma and metabolism of diazepam after chronic alcohol intake.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(1):33-38, 1975.

Very significantly lower concentrations of diazepam at 15 minutes and 1 hour after 10mg intravenous diazepam injection were found in chronic alcoholic patients in comparison to healthy controls. Compared to 13 healthy controls a more rapid elimination of diazepam from the plasma of 14 chronic alcoholic patients during their alcohol free period was observed. The alcoholics had a smaller concentration of the diazepam main metabolite, N-demethyldiazepam, and at 3 hours this difference was significant. The concentrations of free plasma oxazepam as a metabolite of diazepam, were not observed after a single dose of diazepam either in the alcoholics or in volunteers. A more rapid elimination of diazepam after 5mg/kg intraperitoneally in the plasma of rats pretreated with ethyl alcohol (15% in drinking water for 3 weeks) was found than in the control rats. Pretreatment of rats with ethyl alcohol increased significantly the concentration of the hydroxylated metabolite, free oxazepam, in the plasma, but not of the demethylated metabolite, N-demethyldiazepam. 13 references. (Author abstract)

000864 Sellman, R.; Pekkarinen, A.; Kangas, L.; Raijola E. Dept. of Pharmacology, University of Turku, Turku, Finland **Reduced concentrations of plasma diazepam in chronic alcoholics following an oral administration of diazepam.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(1):25-32, 1975.

Diazepam 10mg was given orally to 12 chronic alcoholic patients at the beginning of the alcohol free period and to 14 controls. Diazepam in the plasma was determined gaschromatographically with a 63Ni-EC detector. During the absorption phase the plasma levels of diazepam were reduced to 44% at 2 hours (P less than 0.01) and 32% at 3.5hours (P less than 0.001) in alcoholic patients compared with respective values of normal subjects. The reduced values found in the alcoholic patients may be due to disturbances in the gastrointestinal absorption of diazepam, or to processes involving the portal vein or liver. Some alcoholic patients received a simultaneous treatment with neuroleptics or hypnotics. 14 references. (Author abstract)

000865 Shader, Richard I. Harvard Medical School, Boston, MA **Drug studies with women, the elderly, and groups.** Psychopharmacology Bulletin. 12(3):79-80, 1976.

The psychopharmacological treatment of anxiety is studied. The pharmacokinetic properties of selected clinical drugs and elucidation of variance in response parameters among different subject groups are investigated and surveys of drug usage in hospitalized patients and in residents of the Boston area are conducted. After oral administration of single doses of chlordeazepoxide, there are wide variations in rate of absorption, in the time required for peak blood concentrations to occur and in the peak blood concentrations measured. It is concluded that individual differences in the rate and extent of chlordiazepoxide absorption may account in part for the differences in clinical response to a given dose. Peak concentrations after intramuscular injection are significantly lower and occur later than those following oral administration of the same dose. It is suggested that intramuscular chlordiazepoxide is contraindicated in clinical situations requiring rapid sedation. Studies with intravenous diazepam in hospitalized patients reveal that severe adverse reactions are rare. Unwanted central nervous system depression occurs in approximately 7.1% of all diazepam recipients, the incidence of this effect increases in patients with hypoalbuminemia. Surveys of self-administration of drugs reveal that approximately 20% of the 24,633 respondents use psychotropic drugs. Females use such drugs more frequently than males. Usage is also more prominent in individuals 50-59 years old and in patients with potentially chronic disorders such as neurologic disorders, musculoskeletal disease and ischemic heart disease. Antianxiety drugs, especially diazepam or chlordiazepoxide are taken most frequently; hypnotics, especially barbiturates, constitute the next most widely used drugs. Only 10% of the respondents used antipsychotic agents, antidepressants or CNS stimulants.

000866 Stenberg, Jesper; Wasir, Harbans; Amery, Antoony; Sannerstedt, Rune; Werko, Lars. Department of Medicine I, Sahlgrenska Hospital, S-413 45 Goteborg, Sweden **Comparative hemodynamic studies in man of adrenergic beta1-receptor agents without (H 93/26=metaprolol) or with (H 87/07) intrinsic sympathicomimetic activity.** Acta Pharmacologica et Toxicologica (Kobenhavn). 36(5):76-84, 1975.

The two new cardioselective beta-adrenergic blocking agents H 93/26 and H 87/07 without and with intrinsic sympathicomimetic activity, respectively, were given intravenously to two groups of young healthy men to study the acute influences on systemic hemodynamics at rest and during standardized physical exercise. The findings indicate that H 93/26 exerts marked negative chronotropic effects both at rest and during physical exercise with only moderate negative inotropic effects resulting in significant reductions in cardiac output with no or only minor changes in stroke volume. In the present doses, a negative chronotropic effect of H 87/07 was, on the contrary, discernible first under strenuous physical exercise, the drug exerting no effect on the systemic hemodynamics at rest. It is concluded that the setup used for obtaining hemodynamic data at rest and during physical strain could be a suitable and sensitive instrument to differentiate between various types of beta-adrenergic blocking agents. 2 references. (Author abstract)

000867 Syvalahti, E. Deparment of Pharmacology, University of Turku, Kiinamyllynk. 10, 20520 Turku 52, Finland **The levels of serum growth hormone and immunoreactive insulin after administration of antipyretic analgetics.** Acta Pharmacologica et Toxicologica (Kobenhavn). 37(4):336-344, 1975.

The effects of indomethacin and phenylbutazone suppositories and acetylsalicyclic acid as well as placebo tablets on serum growth hormone, serum immunoreactive insulin and blood glucose concentrations were studied in 41 young male volunteers after an overnight fast. Peak drug concentration in serum was reached 60, 120, and 180 minutes after indomethacin, acetylsalicylic acid and phenylbutazone, respectively. Blood glucose rose after indomethacin and the rise was significant throughout the study. No significant changes in blood glucose were seen after the administration of the other drugs. The levels of serum growth hormone were also significantly increased after indomethacin, but not after the other drugs. The mean of the peak serum growth hormone concentration of the subjects was significantly higher after indomethacin than after the other drugs, which did not differ from each other significantly. There were no significant changes in serum immunoreactive insulin levels after the drugs. However, after acetylsalicylic acid the levels tended to increase and the serum immunoreactive insulin remained significantly higher after acetylsalicylic acid than after placebo. 16 references. (Author abstract modified)

000868 Thiessen, J. J.; Sellers, E. M. ; Denbeigh, P.; Dolman, L. Faculty of Pharmacy, University of Toronto, Toronto, Quebec M56 1A1 **Plasma protein binding of diazepam and tolbutamide in chronic alcoholics.** Journal of Clinical Pharmacology. 16(7):345-351, 1976.

The extent of interindividual variation and the influence of plasma protein concentration on diazepam and tolbutamide binding was studied in humans. The binding of diazepam and tolbutamide was studied by equilibrium dialysis over a total drug concentration range of 1 micrograms/ml to 10 micrograms of diazepam and 50 micrograms/ml to 300 micrograms/ml of tolbutamide in plasma from 21 normal subjects and 14 alcoholic patients with liver disease. At 1 microgram/ml, diazepam plasma protein binding is 98.5% in normal subjects and 97.8% in alcoholics; at 100 microgram/ml, tolbutamide binding is 97.8% in normal subjects and 95.1% in alcoholics. For both drugs at all concentrations, binding to plasma in alcoholics is significantly lower than in normal subjects. Diazepam apparently binds principally to albumin. It is suggested that important changes in pharmacologic effect, distribution, and clearance of diazepam and tolbutamide can be anticipated in alcoholics with hypoalbuminemia. 24 references.

000869 Uchiyama, Toshimitsu; Tsutsui, Sueharu; Ito, Ryuta. Department of Pharmacology, School of Medicine, Toho University, Omori, Tokyo, Japan **New trends of beta-blockers in actions and applications.** Journal of the Medical Society of Toho University (Tokyo). 23(3-4):256-271, 1976.

The history of research into, the classifications of, and the clinical applications of various beta-blockers are reviewed. The theoretical background for the effects of beta interceptors, and the several psychophysiological effects of them are explained. Clinical uses for these drugs in relation to several of the body systems, cardiovascular, endocrine, central nervous, and others are detailed. Side-effects of these drugs are also discussed, and it is pointed out that 75% of these are predictable. 107 references.

000870 Vymazal, J.; Roth, B.; Nevsimal, O. Neurologicka Klinika Fakulty Vseobecneho Lekarstvi, KU, Praha, Czechoslovakia **/Treatment of Parkinsonism with a combination of L-dopa and methyldopa-hydrazine./** Zkusenosti s lecbou parkinsonismu asociaci L-dopy a alfa-methyldopa-hydrazinu. Ceskoslovenska Neurologie a Neurochirurgie (Praha). 39(2):59-62, 1976.

A combination of Carbidopa and L-dopa was administered to 17 patients suffering from Parkinsonism. The therapeutic effect was favorable in 15 patients with 8 excellent results. In 2 patients orofacial hyperkinesia was found. There was intolerance of the drug in 2 cases. It is suggested that the combination of Carbidopa and L-dopa represents the most effective treatment of Parkinsonism at present. 9 references. (Author abstract)

000871 Widerlov, Erik; Sjostrom, Rolf. Forskningskliniken, Ullerakers Sjukhus, S-75017 Uppasala, Sweden **/Thyroid hormone and depression./** Thyreoidea och depression: en oversikt over hormonbehandling vid depressioner med tonvikt lagd pa TRH:s roll som ett eventuellt antidepressivum och diagnosinstrument. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):487-497, 1975.

The antidepressive effect of thyrotropin releasing hormone (TRH) is examined. Results from two double-blind crossover studies with 15 patients showed a significant antidepressive effect of short duration, without any secondary effects. Another double-blind crossover study of 165 patients showed that only a few patients reacted positively to TRH. Experiments with mice showed that TRH had no inhibitory effect on MAO, dopamine, noradrenaline or serotine. Studies on rats showed a 20% increase of (3-methoxy-4-hydroxy-phenylethyl-glygol) (MOPEG) which supports the theory of TRH inducing an increase of noradrenaline in the central nervous system. 15 references.

000872 Yaryura-Tobias, J. A.; Fledel, T.; Neziroglu, F. Research Division, North Nassau Mental Health Center, 1691 Northern Boulevard, Manhasset, NY 11030 **Vitamins, neuroleptics, and antiparkinsonian drugs in catecholamine excretion.** Biological Psychiatry. 11(3):363-366, 1976.

A study designed to observe the action of certain substances (believed to be related to the etiology and treatment of psychosis) on the urninary excretion of dopamine (DA), noradrenaline (NA), and adrenaline (A) is presented. Ten acute and subacute male psychotics with target symptoms of delusions and perceptions underwent drug administrations for six 10 day periods as follows: 1) washout, 2) pyridoxine, 3) niacin, 4) biperiden, 5) tioproperazine, and 6) treatments 4 and 5 combined. At the end of each period, 24 hour urines were collected, and DA, NA and A were separated and measured. Significant differences in the three substances were observed with the administration of pyridoxine, niacin, biperiden, neuroleptics, and neuroleptics combined with biperiden. It is theorized that the combination of pyridoxine and biperiden may have antitherapeutic effects when combined with neuroleptics. 14 references.

14 MECHANISM OF ACTION: BEHAVIORAL

000873 Adams, Anthony J.; Brown, Brian; Haegerstrom-Portnoy, Gunilla; Flom, Merton C.; Jones, Reese T. School of Optometry, University of California, Berkeley, CA 94720 **Evidence for acute effects of alcohol and marijuana on color discrimination.** Perception & Psychophysics. 20(2):119-124, 1976.

A double-blind color discrimination experiment was conducted using placebo and two doses of marihuana to determine their effect on color vision. Significant dose related impairments in hue discrimination on the Farnsworth-Munsell 100 hue test were produced by acute doses of alcohol and marihuana. The impairment of color discrimination was predominantly located in the blue region of the color circle and resembles that seen in acquired color vision defects associated with retinal pathology. The transient nature of the reduced color discrimination raises practical problems in tasks which require stable color perception. 14 references. (Author abstract)

000874 Bach, M. J.; Bruce, D. L. Northwestern University Medical School, Chicago, IL 60611 **An audiovisual test of divided attention.** Perceptual and Motor Skills. 43(1):51-57, 1976.

In a study of the possible behavioral effects of trace anesthetics, a description is given of an audiovisual reaction time task, performance of which was maximal after 15 min. practice and which lasted at this level for 1 week. Sensitivity of the test was shown in an adverse effect of inhalation of traces of anesthetic gases. Comparing responses to auditory and visual stimuli, the control auditory reaction times were faster but were lengthened more in the presence of anesthetics than were the visual ones. This test may be useful in other studies of subtle depressant drug effects. 8 references. (Author abstract)

000875 Bathien, N.; Willer, J.-C.; Hugelin, A. Laboratoire de Physiologie, Faculte de Medecine Saint-Antoine, 27, rue Chaligny, Paris F-75012, France /**Effects of psychotropic drugs on physiological variations and psychometric scores during attention.**/ Effets de drogues psychotropes sur les variations physiologiques et les scores psychometriques au cours de l'attention. Encephale (Paris). 2(1):55-60, 1976.

Effects of activation produced by the association of a difficult task and psychostimulant drugs are examined. The activation profile was determined by measuring heart rates, respiratory rates and Hoffman's reflex (H-reflex) in 10 adult volunteers at rest and during attention tests. Subjects were administered orally liminal doses of diazepam, pyrisuccideanol, fenzolone or amphetamine. After treatment with the psychotropic drugs, psychometric scores decreased in subjects given amphetamine sulfate or fenozolone and reached a level of optimum effectiveness in subjects given pyrisuccideanol. The motor response profile, tested by the H-reflex, varied in the same way as the performance curve. However, cardiac and respiratory rates increased in relation to the activation effect provoked by the drugs. These results demonstrate conditions where performance and physiological activation are dissociated under the effect of psychoactive drugs. 13 references. (Author abstract modified)

000876 Baumler, Gunther. Technische Universitat Munchen, Connollystrasse 32, 8 Munchen 40, Germany /**Influencing achievement motivation through psychotropic drugs: 2. Differential influencing of motivation production with 6 achievement motivation pictures.**/ Beeinflussung der Leistungsmotivation durch Psychopharmaka: II. Differentielle Beeinflussung der Motivproduktion bei den 6 Leistungsmotivationsbildern. Zeitschrift fur Experimentelle und Angewandte Psychologie (Gottingen). 22(3):409-420, 1975.

Effects of methylphenidate (Ritalin) and chlorpromazine (Megaphen) on 72 subjects' responses indicating achievement motivation to six pictures of the Heckhausen Thematic Achievement Motivation Test were analyzed. The following results were obtained: 1) methylphenidate and chlorpromazine increased net hope only in pictures depicting failure, the bipolar hope/fear scale was displaced and hope for success increased and fear of failure decreased because these pictures touch on the sociopsychological problem of conflict between hero and authority figure; 2) chlorpromazine decreased motivational responses more strongly than placebo, but methylphenidate had no effect on overall motivation; 3) pictures depicting hope measured only pharmacologically induced changes in the overall motivation, but not the bipolar factor; 4) chlorpromazine, and to some extent methylphenidate, reduced the number of words produced in all the pictures of the test, indicating loss of contact with reality; and 5) number of words produced during the test, both by subjects receiving drug and those receiving placebo, depended upon warming up effects and fatigue effects. 4 references. (Author abstract)

000877 Bixler, Edward O.; Kales, Anthony; Santen, Richard; Vela-Bueno, Antonio; Soldatos, Constantin R.; Kotas, Kathleen M. Sleep and Research Center, Department of Medicine, Pennsylvania State University, Milton S. Hershey Medical Center, Hershey, PA 17033 **Effects of flurazepam (Dalmane) on anterior pituitary secretion.** Research Communications in Chemical Pathology and Pharmacology. 14(3):421-429, 1976.

The effects of continued administration of flurazepam on sleep stages and release patterns for growth hormone (GH), luteinizing hormone (LH) and prolactin were evaluated in two subjects during a 3 week period. Flurazepam was administered in 30mg doses nightly. Sleep stages were monitored throughout the placebo baseline, drug and placebo withdrawal conditions. Blood samples were obtained on night 3 and 4 of baseline, after 2 and 3 weeks of drug administration and following extended drug withdrawal. Flurazepam produces a marked suppression in stages 3 and 4 (slow wave) sleep which is maintained throughout the drug administration period. Following withdrawal, there is a slight increase in slow wave sleep above baseline levels. No clear cut changes in mean nightly output, pulse amplitude of release and pulse frequency of release GH, LH or prolactin. It is concluded that the decrease in slow wave sleep produced by administering flurazepam 30mg is not accompanied by any clear cut changes in GH, LH or prolactin. 12 references. (Author abstract modified)

000878 Boyd, E. L.; Knapp, Richard B.; Remen, Daniel; Linet, O. I. no address **The comparison of the hypnotic activity of triazolam, diazepam, and placebo in inpatient insomniacs.** West Virginia Medical Journal. 72(8):208, 1976.

A study was carried out to: 1) evaluate the safety and efficacy of triazolam; 2) to compare the relative potency of triazolam to diazepam; and 3) to compare the side-effects of triazolam, diazepam, and placebo in inpatient insomniacs. It is reported that 0.5mg triazolam helps patients sleep significantly more than placebo, 5mg diazepam or 10mg diazepam. Sleep onset is significantly better after 0.5mg triazolam than after 5mg diazepam. Duration of sleep is significantly better after 0.25mg triazolam or 0.5mg triazolam than after 5mg of diazepam, and fewer awakenings occur with 0.5mg triazolam than with 10mg diazepam or placebo. Both triazolam and diazopam are reported to be free of significant side-effects.

000879 Bruck, Connie. no address /**Abuse of Ritalin by Taft City School District.**/ Battle lines in the Ritalin war. Human Behavior. 5(8):25-33, 1976.

A background study is presented of the families involved in a suit against Southern California's Taft City School District

for dosing their children, labeled hyperactive or minimal brain dysfunctioned (MBD), with Ritalin to increase their classroom manageability. National controversy has arisen over the use of psychoactive drugs to modify the troublesome classroom behavior of children labeled, but not diagnosed, as hyperactive, MBD, learning disabled and organic behavior disordered as a result of this class action suit and later similar civil suits.

000880 Burrows, Graham D.; Foenander, George; Davies, Brian; Scoggins, Bruce A. Department of Psychiatry, Clinical Sciences Building, Royal Melbourne Hospital, Victoria 3050, Australia **Rating scales as predictors of response to tricyclic antidepressants.** Australian and New Zealand Journal of Psychiatry (Carlton). 10(1):53-56, 1976.

In order to determine whether rating scales could predict treatment response to tricyclic antidepressants, 53 patients suffering from depressive illness were classified as responders or nonresponders on the basis of an amelioration score of the Hamilton Rating Scale for depression after 6 weeks treatment with nortriptyline hydrochloride at 150mg daily. A multivariate analysis of variance was performed on the four psychological rating sclae scores used. There was a significant difference between the two groups after adjustment for age. subjects were then classified as nonresponders and responders on the basis of their discriminant scores. The prediction of response to tricyclic antidepressants was found to be at 75% probability. 12 references. (Author abstract modified)

000881 Castellani, Alessandro; Lescovelli, Manuela; Perbellini, Dino. no address **/Clinical electroencephalographic modifications of the hypnotic pattern obtained with the use of N-demethyldiazepam in 25 insomniac patients./** Modificazioni clinico-elettroencefalografiche indotte dall'N-demetildiazepam sul pattern ipnico di 25 pazienti psichiatrici affetti da insonnia. Lavoro Neuropsichiatrico (Roma). 56(1/2/3):155-183, 1975.

Following a review of recent research on sleep from the etiopathogenic, semeiological, clinical and electroencephalographic viewpoints a study is reported of changes in EEG obtained with a hypnotic drug. N-demethyldiazepam was administered in doses of 20mg to 30mg/day to 25 psychiatric patients, 23 to 73 years old, presenting sleep disorders of various degrees of severity. Results showed these doses of N-demethyldiazepam produced remarkable effects in reducing the time of sleep onset and promoted and prolonged the REM phases of sleep. 49 references. (Author abstract modified)

000882 Clayton, Andrew B. Dept. of Transportation and Environmental Planning, Univ. of Birmingham, England **The effects of psychotropic drugs upon driving-related skills.** Human Factors. 18(3):241-252, 1976.

The use of psychotropic drugs by drivers is considered to be on the increase, although little accurate epidemiological data are available. The results of laboratory investigations of the effects of barbiturate and nonbarbiturate hypnotics, tranquilizers, and antidepressants upon sensory functions and perceptual skills, cognitive skills, and motor skills are reviewed. The relationship between such skills and actual driving performance is discussed and some possible mechanisms whereby psychotropic drugs may contribute to the causation of accidents are described. In view of the wide variety of drugs, dose levels, and test situations used, few definite conclusions may be drawn regarding the effects of psychotropic drugs upon driving related skills. 54 references. (Author abstract modified)

000883 Cochran, Evelyn; Robins, Eli; Grote, Sylvia. Washington University School of Medicine, Department of Psychiatry, St. Louis, MO **Regional serotonin levels in brain: a comparison of depressive suicides and alcoholic suicides with controls.** Biological Psychiatry. 11(3):283-294, 1976.

A study of the levels of 5-hydroxytryptamine (5-HT, serotonin) in various areas of the human brain in suicides and animal controls is reported. Levels of 5-HT in 33 areas of the human brain were measured and compared in 10 depressed suicides, 9 alcoholic suicides, and 12 controls. The highest concentration of 5-HT was found in substantia nigra and the lowest in frontal gray, but no significant differences were found among diagnostic groups in any of the areas studied. It is concluded that, although no differences were found in identifiable subdivisions of the brain, undetected differences may occur in individual nuclei in the brain. 25 references. (Author abstract modified)

000884 Coleman, Nathan; Dexheimer, Patric; DiMascio, Alberto; Redman, William; Finnerty, Richard. Fuller Memorial Hospital, South Attleboro, MA 02703 **Deanol in the treatment of hyperkinetic children.** Psychosomatics. 17(2):68-72, 1976.

A twelve week double-blind comparison of deanol acetamidobenzoate (Deaner) and a placebo was undertaken with a study population of 50 hyperkinetic children, ages six through twelve. Assessment of drug response and possible side effects were made by a psychiatrist, a pediatrician, a psychologist (using WISC, WRAT and Porteus MAGE tests), the child, the teacher, and the parents. Deanol patients showed beneficial change. 11 references.

000885 Cronholm, B.; Schalling, D.; Levander, S.; Lagergren, K.; Mindus, P. no address **Study of the effects of a new nootropic substance on mental performances (pacemaker patients).** Medicina Psicosomatica (Roma). 20(4):374, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975), paper presented a study of the effects of a new nootropic substance on mental performance in pacemaker patients. Because animal studies and uncontrolled clinical studies have shown that piracetam may improve impaired mental function a series of computerized tests of alertness were developed. Use of these tests has shown that piracetam counteracts the impairment of mental performance induced by a lowered heartrate in pacemaker patients. In a controlled study on aging subjects, piracetam was shown to improve performance on the computerized tests on some pencil and paper tests. (Author abstract modified)

000886 Di Donato, R.; Diodato, S. University of Chieti, Chieti, Italy **/Luscher test and anxiety: variations in chromatic choices while in a state of anxiety./** Test di Luscher e ansia (variazioni delle scelte cromatiche negli stati ansiosi). Medicina Psicosomatica (Roma). 20(3):211-215, 1975.

In a study of the Luscher scale and anxiety, variations in chromatic choices were examined as a function of variations in the levels of anxiety and administration of drugs. Subjects were divided into four groups: placebo, 5mg diazepam, 25mg trazodone, and 50mg trazodone. The double-blind scheme was used, together with the ITAP anxiety scale for determining the state of anxiety in each patient. Results demonstrated the validity of the Luscher test, along with a general improvement in the patients' condition following administration of the drugs. Among the colors, particular emphasis was placed on brown and yellow: the former relating to anxiety, and the latter to the will to live. 2 references.

000887 Dimond, S. J. no address **The effects of a new nootropic substance on the capacity for verbal memory and learning in normal man.** Medicina Psicosomatica (Roma). 20(4):371, 1975.

Results which show that verbal memory and learning may be improved in normal man through the administration of Piracetam (UCB6215) were reported at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). The drug was given to normal volunteers who were tested on a number of learning tasks. It is concluded that subjects taking the drug slowly improved over controls, and after 14 days there was substantial improvement in their capacity for word list learning. It was found also that the overall capacity for handling verbal information on a dichotic listening task had increased, whereas a nonverbal motor learning test showed no change. Results are interpreted as a selective improvement in the capacity for verbal learning. (Author abstract modified)

000888 Eleftheriou, Basil E. no address **Psychopharmacogenetics.** New York, Plenum, 1975. 472 p. $28.00.

The behavioral responses of various drugs that alter or may not alter behavior in genetically defined animal models, or in specified familial human subjects are studied. Research is reported on: 1) behavioral changes induced by apomorphine; 2) effects of anesthetics on learning behavior in genetically defined species; 3) the genetic/behavior/psychological bases on audiogenic seizures; and 4) genetic determinants of behavioral responses to depressant and stimulant drugs.

000889 Evans, M. A.; Martz, R.; Lemberger, L.; Rodda, B. E.; Forney, R. B. Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232 **Effects of dextroamphetamine on psychomotor skills.** Clinical Pharmacology and Therapeutics. 19(6):777-781, 1976.

The effects of graded doses of dextroamphetamine on certain quantitative measures of psychomotor performance in a nonfatigue situation were evaluated. Twelve healthy male volunteers were given 0, 5, 10, 15mg/70kg dextroamphetamine orally in a random double-blind fashion. Blood pressure of the subjects increased linearly with dose while heartrate was unchanged. Although selected individual tests of stance stability and motor function improved in a dose related fashion, a generalized improvement in performance was not found. Delayed auditory feedback testing failed to show improvement in mental performance after dextroamphetamine. It is concluded that administration of dextroamphetamine in a nonfatigue situation does not result in generalized improvement in either mental or motor function. 18 references. (Author abstract modified)

000890 Fischman, Marian W.; Schuster, Charles R.; Resnekov, Leon; Shick, J. Fred E.; Krasnegor, Norman A.; Fennell, William; Freedman, Daniel X. Department of Psychiatry, University of Chicago, 950 E. 59th St., Chicago, IL 60637 **Cardiovascular and subjective effects of intravenous cocaine administration in humans.** Archives of General Psychiatry. 33(8):983-989, 1976.

Nine volunteer subjects were tested for cardiovascular and subjective effects with intravenously administered cocaine hydrochloride in doses ranging from 4 to 32mg, as well as 10mg of dextroamphetamine sulfate. Generally parallel dose effect functions were obtained for heartrate, blood pressure, Addiction Research Center inventory scores, Profile of Mood Scales, and subject ratings. A substantial effect on each of these variables was recorded after 8mg of cocaine. The increase continued and peaked at approximately 16mg after which it usually leveled off. Ten milligrams of dextroamphetamine generally had an effect comparable to 8 to 16mg of cocaine. 26 references. (Author abstract)

000891 Fujii, Shozo. National Sanatorium Tottori Hospital, Japan **Psychiatry, medicine, and sleep -- sleeping drugs and tranquilizers.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(8):901-911, 1975.

To study the effects of barbiturates and nonbarbiturates on human sleep, two separate experiments were conducted on four subjects by administering placebo the first 3 nights, 200mg of amobarbital (AMOB) in the first experiment and 5mg of nitrazepam (NZP) in the second experiment, then followed by placebo the last 2 nights. In the first experiment, with the administration of AMOB, there was a slight increase in the amount of sleep, decrease in sleep latency, increase in stage 2, moderate decrease stages 3 and 4, moderate increase in REMP during the first and third night of AMOB intake, and a moderate decrease in the number and REMP%. In the second experiment, with the administration of NZP, there was an increase in stage 2, moderate decrease in stages 3 and 4, prolonged REMP and a decrease in the number of REMP. 36 references.

000892 Giurgea, C. no address **Experimental pharmacological differential definition of nootropic drugs.** Medicina Psicosomatica (Roma). 20(4):372, 1975.

A report of a differential pharmacological study aimed at situating nootropics among other CNS acting drugs was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Nootropic drugs were defined as drugs aiming primarily, by a functional telencephalic selectivity, at enhancing efficiency of the higher integrative mechanisms of the brain. The clinical efficiency of Piracetam and its unusual neuropharmacology were described as: 1) enhancing learning and memory abilities; 2) protecting against aggressions to the brain; 3) facilitating interhemispheric flow of information; and 4) lacking neurovegetative, reticular, or rhinencephalic interferences, as well as sedative or analeptic properties. (Author abstract modified)

000893 Gowardman, M.; Brown, R. A. Kingseat Hospital, Papakura, New Zealand **Dibenzepin and amitriptyline in depressive states: comparative double-blind trial.** New Zealand Medical Journal (Dunedin). 83(560):194-197, 1976.

The therapeutic efficacy of dibenzepin is compared with amitriptyline in mild and moderately severe depressive reactions to establish if it was superior in controlling any particular type of target symptom or depressive reaction. Side-effects and toxic reactions of both drugs were evaluated. A double-blind trial was designed with ten patients assigned randomly to each drug. The Zung self-rating depression scale was used to rate drug effectiveness. Both drugs appeared to have similar pharmacological profiles, but dibenzepin appeared slightly preferable in neurotic depressives, mainly because of less frequent and less severe side-effects. 8 references.

000894 Grant, Igor; Mohns Lynn; Miller, Michael; Reitan, Ralph M. Department of Psychiatry, University of California, San Diego, M-003, La Jolla, CA 92093 **A neuropsychological study of polydrug users.** Archives of General Psychiatry. 33(8):973-978, 1976.

In a study of the long-term effects of persistent nonmedical drug use, 22 young men, all extensive polydrug users, were

examined while free from drugs for an average of 60 days by means of the Halstead-Reitan Neuropsychological Test Battery. Drug use inventory included cigarettes, alcohol, marijuana, volatiles, mescaline, LSD, cocaine, amphetamines, barbiturates, and other sedatives and narcotics. Their performance was compared to that of age/education/sex/matched neurologically intact medical patients and a similarly matched group of neurologically impaired patients. Blind independent ratings of test protocols by two experienced clinicians judged 41% to 64% of the drug users, 11% to 26% of the medical patients, and 84% to 89% of the neurologic patients to be impaired. Interpretation of these results suggests that in some individuals, heavy polydrug use may be associated with neuropsychological dysfunction, which persists at least an average of 2 months beyond cessation of drug use. 34 references. (Author abstract modified)

000895 Gross, Leon J. Center for Educational Development, Un. of Ill. College of Medinine, 835 S. Wolcott Ave., Chicago, IL 60612 **Drug-induced handwriting changes: an empirical review.** Texas Reports on Biology and Medicine. 33(3):371-390, 1975.

Experiments examining the relationship between specific pharmacological agents, such as anti-Parkinsonian and antipsychotic drugs, and postingestion handwriting alterations are reviewed in order to analyze the basic experimental design components. Discussion of experimental inadequacies in the cited literature is given, and the inherent use of handwriting graphomotor indices such as speed, accuracy, rhythm and size are considered to be measurable only by the researchers' subjective standards. Alcohol effects on handwriting studies show insufficient uniformity of design. The literature reveals significant discrepancies in individual susceptibilities by groups (alcoholics vs nonalcoholics) to drug induced graphomotor reactions. It is assumed that any agent affecting the nervous system should logically produce alterations in one's typical pattern of writing and the documented research literature supports this contention, particularly studies dealing with neuroleptic agents and L-DOPA which have revealed systematic and reliable handwriting changes. The potential of assessing handwriting changes as a valuable criterion in biomedical and pharmacological research is emphasized. 36 references.

000896 Hartmann, Ernest; Cravens, James. Sleep and Dream Laboratory, Boston State Hospital, IRR Building, 591 Morton Street, Boston, MA 02124 **Sleep: effects of d- and l-amphetamine in man and in rat.** Psychopharmacology (Berlin). 50(2):171-175, 1976.

The effects of dextroamphetamine and levoamphetamine on polygraphically recorded sleep were studied in humans and in rats. In both species, dextroamphetamine produces a significantly greater increase in waking time than does levoamphetamine. Also in both species, the two isomers have equal effects in reducing desynchronized sleep time. It is suggested that dopamine plays a direct role in wakefulness while norepinephrine is related inversely to amounts of desynchronized sleep. 44 references. (Author abstract modified)

000897 Hata, Sekishi. Department of Neuro-psychiatry, Tottori University School of Medicine, Japan **Psychiatric medicine and sleep -- chlorpromazine.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(8):914-920, 1975.

Characteristic effects of chlorpromazine (CPZ) and reserpine on human sleep are examined. From the studies conducted on CPZ on REM sleep by J. Toyoda, Y. Fujitani, S. Lewis, D. J. Kupfer and others, it is observed that conclusions vary due to varying methods, dosages and subjects used. It is seen that although CPZ is weaker than the barbiturates, it induces more natural sleep than barbiturates. Studies conducted on reserpine show that it causes increased REM sleep, decreases stages 2 and 4, increases intermittant awakening periods and anxiety, and has some harmful effects on human sleep. The effects of other antipsychotic drugs such as phenothiazine and haloperidol are also mentioned. 35 references.

000898 Hendel, J.; Elsass, P.; Andreasen, P. Buch; Gymoese, E.; Hvidberg, E. F. Clinical Pharmacology Research Unit, Rigshospitalet 9 Blegdamsvej, DK-2100 Copenhagen, Denmark **Neuropsychologic effects of diazepam related to single dose kinetics and liver function.** Psychopharmacology (Berlin). 48(1):11-17, 1976.

The neurophysiologic and neuropsychologic effects and their relation to the kinetics of diazepam (DZ) were studied in 10 patients with impaired liver function of various degrees and in three normal subjects after 10mg DZ i.v. The plasma concentration data were treated according to a two compartment open model. Neurophysiologic effect measurements were obtained from galvanic skin response, continuous reaction times (CRT), heartrate, and averaged evoked potentials; neuropsychologic measurements were obtained from trail making A + B, hidden pattern, word fluency, and subtraction tests. In addition, clinical effects were rated by Beechers Mood Scale and Spielbergers Anxiety Scale. Except for trail making A and word fluency, all tests discriminated well between the experimental conditions with or without diazepam. No difference from normal in the response to acute diazepam administration could be detected in patients with reduced liver function. A linear correlation between prolongation in CRT and DZ log plasma concentration was demonstrated in the entire, heterogenous patient material. In the clinical ratings only items of a predominantly sedative and autonomic significance responded to the diazepam injection, while predominantly anxiolytic items did not. 11 references. (Author abstract)

000899 Hiep, Albert; Marriott, Peter. Modecate Clinic, Royal Park Psychiatric Hospital, Melbourne, Australia **Long-acting neuroleptics -- a fairy story?** Nursing Times (London). 72(22):863-866, 1976.

Experiences of 3 years followup treatment at an Australian outpatient clinic for schizophrenic patients on Modecate therapy are described and indications of differing problems in Australian from those in England are presented. Charts and descriptions are included of the flow of the clinic routine; the distribution differential schizophrenic diagnoses over Australian migrant population within the clinic; and the length of hospital stays before and after treatments. Outpatient care is coupled with community health nursing which provides maintenance visits and assessments in the patient's own home. The community nursing program has been effective in keeping the patients out of the hospitals and in hospital/community/patient/family liason. The concept of "total patient care" combining psychotherapy, family therapy, community nursing visits and chemical restraints of psychopathic episodes is seen to be effective. 12 references.

000900 Hindmarch, Ian. Department of Psychology, University of Leeds, Leeds, England **Benzodiazepines and human performance.** Bulletin of the British Psychological Society (London). 28:237, 1975.

The effects of both acute and chronic administration of benzodiazepine derivatives on psychological aspects of performance in normal human volunteers is discussed. Evaluative studies assessing the effect of the drugs on complex cognitive and psychomotor performance in every day situations are reviewed. These studies are essentially concerned with the safety of benzodiazepines in normal medicinal use and with possible detrimental effects on performance resulting from drug use under normal prescribing conditions. Laboratory studies where the change in performance measures following administration of a benzodiazepine derivative is correlated with basic physiological variables are also summarized. Many are correlative studies to understand the mechanisms of benzodiazepine action in man relating behavioral action to underlying physiological variables. The importance of both evaluative and correlative approaches is emphasized in view of the widespread prescription of the drugs to individuals habitually indulging in complex performance tasks and the greater interindividual and intraindividual variation in effects. 3 references. (Author abstract modified)

000901 Hirose, Tetsuya. Shinkei Kenkyujo Seiwa Hospital, Japan **Treatment of insomnia.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(8):881-887, 1975.

Methods of treating insomnia, including K. Vogtherr's use of imagination and J. H. Schultz's hypnotic training method to induce sleep, as well as pharmacological treatment methods are discussed. Important features of tranquilizers (diazepam, cloxazolam, medazopam, chlordiazepoxide), barbiturates and nonbarbiturates, antipsychotic drugs (chlorpromazine, levomepromazine) are discussed. The beneficial and harmful effects of using more than one sleeping drug and the treatment of insomnia for depressives are also mentioned. Accurate diagnosis of the causes of insomnia and the degree of insomnia are emphasized. 17 references.

000902 Isozaki, Hiroshi; Tanaka, Masatoshi; Inanaga, Kazutoyo. Department of Central Clinical Laboratory, Kurume University School of Medicine, Kurume, Fukuoka, Japan **Effect of a triazolobenzodiazepine derivative, estazolam, on all-night sleep pattern.** Current Therapeutic Research. 20(4):493-509, 1976.

The effects of estazolam, a new triazolobenzodiazepine, was studied on the all-night sleep pattern in four healthy volunteers. The effects were investigated polygraphically in comparison with those of nitrazepam and placebo by a double-blind crossover method. Four male subjects received placebo orally on the first and second nights and then received either estazolam or nitrazepam on the third night, followed by placebo on the fourth. Statistically significant changes were as follows: 1) administration of estazolam caused a prolongation of total sleep time, a shortening of stage 1 sleep, and a prolongation of stage 2 sleep and of REM latency; 2) nitrazepam caused a prolongation of total sleep time and state 2 sleep, a decrease in frequency of awakening, and a shortening of total waking time during the night. 5 references. (Author abstract modified)

000903 Kodluboy, Donald William. University of Minnesota, Minneapolis, MN 55455 **(Ph.D. dissertation). The effects of d-amphetamine on reading by normal adult human subjects under ratio and interval reinforcement schedules. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. Mfilms, No. 76-14993 HC$15.00 MF$8.00 81 p.

Three doses (0.0375mg/kg, 0.075mg/kg, and 0.15mg/kg) of d-amphetamine sulfate were given to adult human subjects to determine its effects on reading under ratio and interval schedules of reinforcement. The subjects were trained to press a microswitch, the closure of which resulted in the presentation of one line of text projected on a plain surface in front of the subject. Different rates of responding were generated by the fixed ratio (FR) and variable interval differential reinforcement of low rates (VI-DRL) contingencies, thus, there were different interresponse time distributions under the two contingencies. The effect of the drug was a dose related increase in rate of responding under the low rate generating VI-DRL schedule at 0.075mg/kg and a decrease at 0.15mg/kg of d-amphetamine. The effect of the drug or number of inappropriate or premature responses under the VI-DRL schedule was similar. No statistically significant effect was observed due to drug on FR responding. The data support previous literature reports that doses of amphetamine which affect low rates of responding do not affect high rates of responding. (Journal abstract modified)

000904 Lipper, Steven; Tuchman, Michael M. Department of Psychiatry, North Carolina Memorial Hospital, Chapel Hill, NC 27514 **Treatment of chronic post-traumatic organic brain syndrome with dextroamphetamine: first reported case.** Journal of Nervous and Mental Disease. 162(5):366-371, 1976.

A case study is presented of treatment with dextroamphetamine of a young adult accident victim with chronic organic brain syndrome. It is believed that d-amphetamine was critical to the resulting marked diminution in confusion, paranoia and deficit in short-term memory. This was confirmed by the occurrence of a relapse coincident with placebo administration as part of a double-blind evaluation. Amitriptyline appeared to potentiate the therapeutic effects of d-amphetamine. It is concluded that the results achieved, although observational and subjective in nature, warrant replication in controlled, quantitative clinical studies. 14 references. (Author abstract modified)

000905 Manzin, E. Centro di Rianimazione e Cure Intensive dell'Ospedale Civile di Padova, Padua, Italy **/Use of noonaleptic and nootropic drugs in resuscitation./** Impiego di nooanalettici e di nootropi in rianimazione. Medicina Psicosomatica (Roma). 20(4):372-373, 1975.

Resuscitation effects of nooanaleptic and nootropic drugs were discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). (Rome, September, 1975). The resuscitation effect of these drugs was studied in 250 patients. Other reasearch was done at the same time, including: 1) analysis of the variations in sleep time; 2) study of the cerebral blood flow and cerebral metabolism in 20 patients before and after nootropic drugs were administered; and 3) direct comparison between groups of 30 patients receiving drug therapy and the other receiving nootropic drugs. It is concluded that administration of nootropic drugs to comatose patients may be justified because even a marginal reduction in coma time significantly diminishes the risk to the patient.

000906 McKim, W. A. Department of Psychology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada **The effects of pre-exposure to scopolamine on subsequent drug state discrimination.** Psychopharmacology (Berlin). 47(2):153-155, 1976.

In order to test the prediction that preexposure to a drug state would increase the discriminability of that drug state when used as a cue in a discrimination task, eight rats were preexposed to scopolamine for 20 days and eight rats were

given saline injections. The drug preexposed animals acquired a drug state discrimination more quickly than the controls. A difference was also found between the generalization gradients for each group with the preexposed group showing a steeper generalization gradient. 12 references. (Author abstract)

000907 Mendelson, Jack H.; Kuehnle, John C.; Greenberg, Isaac; Mello, Nancy K. Alcohol and Drug Abuse Research Center, McLean Hospital, 115 Mill Street, Belmont, MA 02178 **Operant acquisition of marihuana in man.** Journal of Pharmacology and Experimental Therapeutics. 198(1):42-53, 1976.

Operant work for marihuana cigarettes or money and the effects of marihuana smoking on behavior were examined in 12 casual and 15 heavy marihuana users. Male volunteers were studied in groups of four on a clinical research ward and each subject served as his own control. A 5 day base line period was followed by a 21 day marihuana available period and a 5 day postmarihuana control period. Subjects could earn one 1g marihuana cigarette or 50 cents by 30 minutes of substained performance on a simple operant task. All casual and most heavy user subjects gradually increased marihuana smoking through time. The heavy users smoked more (4.3-6 cigarettes/day) than the casual users (2-3/day). Both groups worked between 2 and 5 times as many hours per/day as was necessary to earn the number of cigarettes smoked. Consequently, subjects earned and saved far more money than was spent for marihuana. The heaviest smokers worked between 6.7and 14.4hours/day, every day. Periods of maximal work coincided with periods of maximal smoking, i.e.,between 4 p.m. and 12 midnight each day. Delayed effects of marihuana dose on points earned the following day showed a dose related decrement in operant work output. In the heavy user group, operant performance decreased sharply 24 hours after three cigarettes/day were smoked, then remained relatively stable after three to eight cigarettes daily and decreased further on the few occasions when more than eight cigarettes were smoked. In the casual user group, the largest 24 hour delayed changes in performance occurred after the smoking of between 1 and 2 and 3 and 4 marihuana cigarettes. No subject stopped operant work even when he smoked 10 or more marihuana cigarettes per day. These data do not support the hypothesis that marihuana induces an "amotivational" syndrome. 35 references. (Author abstract)

000908 Murray, Joseph N. Department of Counseling and Personnel Services, Kent State University, Kent, OH 44242 **Is there a role for the teacher in the use of medications for hyperkinetics?** Journal of Learning Disabilities. 9(1):30-35, 1976.

Determination of the type of intervention to be used in management of the hyperkinetic child is discussed with relevance to the teacher's role. It is suggested that the cause of certain characteristics of the overactive behavior of a child should be a determinant of intervention, differentiating between organic and environmental causation. The special responsibilities of a teacher to a child in class who is hyperkinetic include keeping anecdotal records to objectify behavior descriptions prior to neuroleptic treatment and to allow for reassessment of behavior after the prescriptive program begins, whether it be medication or some form of behavior modification. Educators and school psychologists also have the responsibility of conferring with parents in the event of suspected hyperkinesis in order to suggest professional intervention after school routine interventions have proven unsuccessful. If drug therapy is begun, a policy should be established informing the teacher of the medication in detail so that its use and possible abuse can be monitored intelligently by the teacher. It is concluded that while amphetamines, stimulants, and other types of drugs are not cure alls for all hyperkinetics, they can help some; and the classroom teacher is in a good position to initiate action leading to this type of intervention where necessary by daily observation and appropriate communication with parents. 10 references. (Journal abstract modified)

000909 Ohkuma, Teruo; Hata, Hiroyuki; Fujii, Shozo. Dept. of Psychiatry, Tohoku Medical School, Japan **Differential effects of chlorpromazine, imipramine, nitrazepam, and amobarbital on REM sleep and REM density in man.** Psychiatria et Neurologia Japonica (Tokyo). 77(7):538, 1975.

Some drugs used in the treatment of mental illness and which have an effect on the sleep of the user were studied. To test these effects, several drugs: chlorpromazine (CPZ), imipramine (IMP), nitrazepam (NZP), and amobarbital (AMOB) were administered to five normal males and their percent of REM per REM sleep period and the density of frequency of their REM were observed. For 25mg of CPZ, no discernible effect on REM and percentage of REM was noted. In the case of 25mg of IMP, after 3 nights, there was a marked decrease and disparity in the density of both REM and REM period. For 5mg of NZP, the density of REM percentage of to REM time decreased proportionately. For 200mg of AMOB there was some decrease in the percent of REM , but little effect on REM period. Thus by measuring the percentage REM, the REM density, and the number of REMs the similarities and the differences between various drugs can be discerned.

000910 Peck, A. W.; Adams, R.; Bye, C.; Wilkinson, R. T. Wellcome Research Labs., Langley Court, Beckenham, Kent, BR3 3BS, England **Residual effects of hypnotic drugs: evidence for individual differences on vigilance.** Psychopharmacology (Berlin). 47(2):213-216, 1976.

Twelve healthy volunteers were given butobarbitone 100mg and 200mg, nitrazepam 5mg and 10mg and 2 lactose dummy treatments, at 23.00 hours at weekly intervals over 6 weeks according to a balanced design and using double blind conditions to test the effect of these hypnotics on vigilance. Performance was studied between 09.00 hours and 17.00 hours the following day. Significant impairment of tapping rate and digit symbol substitution occurred. No significant differences occurred between performance after active drug and dummy in auditory vigilance, and subjective effects. Examination of individual differences in the response of subjects to the four hypnotic drug treatments, compared with their responses after dummy, indicated that subjects could be divided into two groups. One group consistently rated themselves as more alert after hypnotics and their vigilance performance improved. The other group consistently were more drowsy after hypnotics and their performance was impaired. It is suggested that the improvement in the first group resulted from improved sleep quality sufficient to counteract the residual effect of the hypnotic, whereas the second group merely showed the residual effects of the drugs. 18 references. (Author abstract)

000911 Post, Robert M.; Kopanda, Richard T. Adult Psychiatry Branch, National Institute of Mental Health, Bldg. 10, 9000 Rockville Pike, Bethesda, MD 20014 **Cocaine, kindling, and psychosis.** American Journal of Psychiatry. 133(6):627-634, 1976.

The evidence indicating that repetitive administration of central nervous system stimulants and other compounds may be associated with progressively increasing effects on pathologi-

cal behavior and seizures rather than tolerance is reviewed. It is suggested that the progressive effects of these compounds may be related to electrical kindling, a phenomenon in which repetitive subthreshold stimulation of the limbic system is eventually associated with major motor seizures. Studies supporting a pharmacological kindling mechanism are reported. A kindling model for psychological stimuli that combines neurophysiological, biochemical, and psychological perspectives is suggested. 100 references. (Author abstract)

000912 Riddle, K. Duane; Rapoport, Judith L. Georgetown Univ. School of Medicine, Dept. of Pediatrics, Georgetown Univ. Hospital, 3800 Reservoir Rd., N.W., Washington, DC 20007 **A 2-year follow-up of 72 hyperactive boys: classroom behavior and peer acceptance.** Journal of Nervous and Mental Disease. 162(2):126-134, 1976.

A 2 year prospective followup of 72 hyperactive boys is reported which examines classroom and home behavior, academic achievement, peer status, and depressive symptomology for patients and a matched control group. Sixty five percent of the sample was still on medication at followup. The patient group continued to manifest behavioral and academic difficulty. Off drug classroom behavior showed considerable stability from baseline to 2 year followup which did not appear to be significantly influenced by change of school or interim stimulant drug treatment. Academic difficulties, low peer status and depressive symptoms exceeded that of the control group. Low peer status at 2 years was predicted for the patient group by baseline (but not current) classroom hyperactivity. The continued difficulties for this middle-class sample, in spite of faithful stimulant drug intake, ancillary educational and psychiatric support, are disappointing. However, as no untreated comparison group was available, the relative benefit of continued drug treatment could not be directly examined. Some indirect evidence, however, indicates that although drugs may continue to have a suppressant effect on impulsive and hyperactive behavior, peer status and academic achievement may not be improved. An optimally medicated group randomly assigned had almost identical academic achievement and social acceptance as did a group of dropouts from drug treatment or the sample as a whole. 24 references. (Author abstract modified)

000913 Riley, Anthony L.; Jacobs, W. J.; LoLordo, Vincent M. Department of Psychology, American University, Massachusetts and Nebraska Avenues, N.W., Washington, DC 20016 **Drug exposure and the acquisition and retention of a conditioned taste aversion.** Journal of Comparative and Physiological Psychology. 90(8):799-807, 1976.

Two experiments examined the effects of preexposure and postexposure to a drug on the acquisition and retention of a conditioned taste aversion induced by that drug. Experiment 1 demonstrated that although drug preexposure attenuated a subsequent conditioned aversion, repeated taste drug pairings reversed the initial attenuation effect and resulted in nearly complete avoidance of consumption. Experiment 2, however, demonstrated that drug postexposure did not alter a previously established conditioned aversion, although the postexposure experiences were effective in attenuating a conditioned aversion to a second novel solution. It was suggested that conditioned aversions are mediated by ACTH and that preexposure to a drug results in tolerance to that drug, yielding a smaller ACTH response and thereby a weaker aversion. 29 references. (Author abstract)

000914 Roquefeuil, B.; Escuret, E. no address **/Study of nooanaleptic drug effect on brain metabolism in humans./** Etude d'un nooanaleptique sur le metabolisme cerebral en clinque humaine. Medicina Psicosomatica (Roma). 20(4):373, 1975.

Use of nooanaleptic and nootropic drugs was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). The nootropic substance piracetam was used to accelerate turnover in autogenic training therapy. The biochemical substratum of piracetam's action causes acceleration of macromolecular synthesis, especially in intracerebral areas. In an experimental study heavy doses of piracetam given to severely comatose patients resulted in an appreciable increase in intracerebral metabolism in about 2/3 of the patients.

000915 Saletu, B.; Matejcek, M.; Knor, K.; Ferner, U.; Schneewind, U. Section of Pharmacopsychiatry, Psychiatrische Universitatsklinik Wein, Wahringergurtel 74-76, A-1090, Vienna, Austria **Assessing the psychoactivity of cloxazolam (MT 14-411) by quantitative EEG and psychological studies.** Current Therapeutic Research. 20(4):510-528, 1976.

The psychoactive properties of cloxazolam, a new benzodiazepine, as compared with diazepam and placebo are reported, as determined in a double-blind study involving eight healthy volunteers. Power spectral density analysis of a resting EEG demonstrated no significant changes after placebo. In contrast, both diazepam and cloxazolam produced an EEG profile characterized by an increase of beta and a decrease of alpha activity, which is typical for anxiolytic drugs. Cloxazolam produced a more pronounced sedative effect than diazepam in the same dosage range. Pulse rate and blood pressure did not reveal any statistically or clinically significant changes. Evaluation of the semantic differential (affect polarity profile) demonstrated that, in contrast to placebo and diazepam, cloxazolam dosages attenuated significantly wakefulness, which in its time course correlated with the EEG parameters. Extroversion was attenuated only after higher dosages of cloxazolam, which was reflected again in the neurophysiological parameters. Mood was not significantly altered by any of the substances, nor were there any drug specific changes in concentration. 19 references. (Journal abstract modified)

000916 Schmidt, T. H.; Schonecke, O. W.; Herrmann, J. M.; Krier, N.; Krull, F.; Selbmann, H.; Schafer, N.; Werner, I. no address **Psychophysiological investigation of the influence of various psychological conditions and propranolol on haemodynamic cardiovascular parameters in hypertensive patients.** Medicina Psicosomatica (Roma). 20(4):407-408, 1975.

A study of haemodynamic parameters (systolic and diastolic blood pressure, heartrate, cardiac output, stroke volume and total peripheral resistance) which were assessed in 30 hypertensive patients was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Patients were observed at 1 minute intervals, in the psychological situation of solving certain tasks before and after i.v. administration of 2mg propranolol. Lacey's hypothesis concerning differing cardiovascular reactions to different situations was tested and extended haemodynamically. Four tasks were set involving internal problem-solving (mental arithmetic, sentence construction) or receiving environmental inputs with and without demands for cognitive elaboration (spotting picture errors, stroboscope). Data were evaluated statistically by analysis of variance. It was concluded that certain haemodynamic cardiovascular reaction patterns appear in conjunction with the respective types of task situation and are

accordingly differently influenced by propranolol. (Author abstract modified)

000917 Schupp, Robin Rody. Illinois Institute of Technology, chicago, IL 60616 **The effect of methylphenidate on cognitive and behavioral functioning in a selective population of hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-13167 HC$15.00 MF$8.50 114 p.

The effects of methylphenidate (Ritalin) on cognitive and behavioral functioning in hyperactive White males between the ages of 8 and 12 years were investigated. Dosages varied from 10 to 65mg per day in a double-blind design. Hyperactive subjects were also assigned to placebo group, and 12 normal controls were included. Instruments included the Children's Embedded Figures Tests, the Halstead-Reitan Category Test, and the Matching Familiar Figures Tests, plus the Werry and Sprague Activity Rating Scale, and the Peterson-Quay Behavior Problem Checklist. Teachers completed the Conners' Abbreviated Teacher Rating Scale. Data suggest that improvement in behavior and cognitive abilities from methylphenidate may result from a general increase in attention, response organization, and impulse control. The effects rapidly dissipate (within a 3 day period) after being taken over a prolonged period (3 months). Hyperactives receiving the drug were rated more aggressive and more of a behavior problem than normal controls. Teachers reported children receiving Ritalin disturbing to more attentive, less fidgety, and less disturbing to other subjects. Mothers could generally identify the drug from the placebo condition. Learning difficulties continued after drug treatment, and remediation is suggested for use in conjunction with medication. (Journal abstract modified)

000918 Skaug, Odvar E. Sentrallaboratoriet, Lier Sykehus, 3400 Lierbyen, Norway **/Serum concentrations of triimipramine in healthy subjects./** Serumkonsentrasjoner av triimipramin (Surmontil) tilfort henholdsvis som maleat og embonat til friske forsokspersoner. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(6):453-459, 1975.

A gas chromatographic method for determining triimipramine (Surmontil) and its desmethylated compounds in blood serum is described in a study involving six persons. A gas chromatograph equipped with nitrogen detector was used to obtain a high sensitivity for the two compounds. After oral intake of triimipramine as maleate or embonate the two compounds are equally well absorbed judged by the serum concentrations of the drugs. Effects such as increased appetite, tiredness and restlessness were reported from all participants in experiment. The somatic and psychic symptoms lasted for 30-40 hours from a single dose of 100-150mg triimipramine. 2 references. (Author abstract modified)

000919 Soulairac, A. A.; Soulairac, M. L. no address **/Study of the effects of a new nootropic substance on cardiac and cerebral metabolism./** Recherches sur les effects d'une nouvelle substance nootrope sur le metabolisme cerebral et cardiaque. Medicina Psicosomatica (Roma). 20(4):374, 1975.

The effect of piracetam on brain and heart was discussed at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). The metabolic effects of piracetam on the cardiac and cerebral regions of the body was studied by electrocorticographic and EKG responses during autogenic training. A study of the effects of piracetam used alone or in association with a chronic alcoholization in the rat showed marked effect on the reappearance of cortical electrogenesis after its postanoxia loss. Piracetam significantly increased the duration of cardiac resistance under anoxia. It was concluded that Piracetam is an important drug which can have a good effect on the cerebral and cardiac metabolism.

000920 Stricherz, Mathias E.; Pratt, Peter. Texas Tech University, University Counseling Center, Box 4160, Lubbock, TX 79409 **Betel quid and reaction time.** Pharmacology Biochemistry and Behavior. 4(5):627-628, 1976.

The effects of betel quid (betel nut, piper leaf, and calcium hydroxide) chewing on simple reaction time latencies was studied in 15 Yapese subjects. The entire quid produces discernible behavioral effects that are manifested in a relatively short time period following quid ingestion. Reaction time latencies lengthen following quid ingestion during the first 20 reaction time trials or within an apparent initial 5 minute interval. Ingestion of partial quid (nut and leaf only) has no significant effect on reaction time latencies. It is suggested that the entire quid is needed to produce discernible effects. 5 references. (Author abstract modified)

000921 Suchenwirth, R. no address **Effects in clinical neurology of therapy with nootropic agent.** Medicina Psicosomatica (Roma). 20(4):374-375, 1975.

Results of the treatment of over 100 patients with the nootropic agent piracetam were presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). In most cases the product was given orally, in severe cases intraveneously. Good results on concentration, memory and critical reasoning, and possibly on vigilance, orientation, psychomotor condition and mood were observed by the patients themselves, the investigator and others. It was concluded that the drug seems to exert a favorable effect in cases of head injuries, cerebral arteriosclerosis, all kinds of edema and in cerebral intoxication. Highly acute processes were difficult to assess because an open study was done, and it was difficult to differentiate an average effect from spontaneous alterations. In chronic processes with no cellular substrate left, definite results could be seen. Increased agitation and irritation are possible side-effects. Piracetam, it is further concluded, seems to offer a new approach to the treatment of reversible cerebral disorders, especially "transitional" syndromes which so far have been beyond any effective therapy. (Author abstract modified)

000922 Swanson, James M.; Kinsbourne, Marcel. Neuropsychology Research Unit, Research Institute, Hospital for Sick Children, Toronto, Ontario M5G 1X8, Canada **Stimulant-related state-dependent learning in hyperactive children.** Science. No. 4246:1354-1357, 1976.

Hyperactive and nonhyperactive children performed a learning task in two states, while being treated with stimulant medication (methylphenidate) and while taking a placebo, and were tested for retention of each class of learned material in both states. Symmetrical state-dependent learning was demonstrated in the hyperactive group but not in the nonhyperactive group. The state-dependent effect was contingent on the presence of drug induced facilitation during initial learning. This is apparently the first report on record of state-dependent learning with a drug agent that facilitates rather than impairs performance of human subjects. 39 references. (Author abstract)

000923 Takahashi, Yasuro; Takahashi, Kiyohisa. Tokyo-to Shinkei Kagaku Sogo Kenkyujo, Japan **Effects of antidepressants upon sleep, especially on REM sleep.** Japanese Journal of Clinical Psychiatry (Tokyo). 4(8):921-936, 1975.

REM sleep mechanism and the effects of antidepressants on REM sleep in normal, depressive, and narcoleptic subjects are discussed. Research findings on the effects of tricyclic antidepressants (clomipramine, imipramine, amitriptyline), monoamine oxidase inhibitors (phenelzine, hydrazine, tranylcypromine) and psychostimulants (amphetamine, methylphenidate, phenmetrazine) on REM sleep are presented. 51 references.

000924 Taylor, Stuart P.; Vardaris, Richard M.; Rawtich, Allen B.; Gammon, Charles B.; Cranston, Jay W.; Lubetkin, Arvin I. Department of Psychology, Kent State University, Kent, OH 44242 **The effects of alcohol and delta-9-tetrahydrocannabinol on human physical aggression.** Aggressive Behavior. 2(2):153-161, 1976.

Forty male undergraduates were provoked to aggression following their ingestion of high or low doses of either alcohol or delta-9-tetrahydrocannabinol (THC). The expression of physical aggression was related to the quantity of alcohol ingested. The high dose of alcohol instigated more intense aggression than the low dose. The high dose of THC, on the other hand, did not increase aggressive behavior. In fact, it tended to produce a weak suppression effect. 13 references. (Author abstract)

000925 Weissman, Myrna M. Depression Research Unit, Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06519 **Psychotherapy and behaviour therapy.** Lancet (London). 2(7975):45, 1976.

Similarities in positive findings of studies of two kinds of treatment for depression are reported. One study shows results of treatment with psychotherapy -- individual, group, marital. The second uses drug therapy. Sample generally includes neurotic depressives and not psychotic depressives or bipolars. The drugs used were tricylic antidepressants, amitriptyline and imipramine. The psychotherapy study charts the place, time, type of treatment, outcome of treatment and reference. The drug study indicates place, length of maintenance, drugs, effect of antidepressants, reference. Conclusion states there is a strong argument for combination treatment of drugs and psychotherapy. 8 references.

000926 Werry, J. S. Department of Psychiatry, School of Medicine, University of Auckland, Private Bag, Auckland, New Zealand **Medication for hyperkinetic children.** Current Therapeutics (Milford). 17(4):11-12,15,18,21,22,24, 1976.

The hyperkinetic syndrome is a symptom complex of hyperactivity, short attention span, distractibility, impulsivity, learning difficulties, other behavior problems and "equivocal" neurological signs. However, none of these terms has ever been objectively defined and at present diagnosis is largely a matter of clinical judgement. In the management of the disorder, drugs do have a place but the decision to use medication is a complex procedure diagnostically and therapeutically calling for the highest in clinical skill and medical supervision. The most useful medication at present is the stimulant group of drugs, particularly dextroamphetamine and methylphenidate. Antipsychotic drugs are sometimes useful but carry the risk of depressing higher CNS functions such as attention and cognition. Other drugs which have been shown to be of value include tricyclic antidepressants (although their effect is less predictable and less striking than that of the stimulants) and pemoline. (Author abstract)

000927 Werry, J. S.; Aman, M. G.; Lampen, Eileen. Department of Psychiatry, School of Medicine, University of Auckland, Auckland, New Zealand **Haloperidol and methylphenidate in hyperactive children.** Acta Paedopsychiatrica (Basel). 42(1):26-40, 1976.

A double-blind crossover study of two doses of haloperidol (0.025mg/kg and 0.05mg/kg, methylphenidate (0.3mg/kg) and identical inert placebo was carried out in 32 children aged 5 through 10 years diagnosed as either hyperkinetic or unsocialized aggressive. Drugs were given for 3 weeks at a time, drug order being randomized across subjects by use of a Latin square. A variety of teacher, parent, psychiatrist and laboratory derived measures of behavior and physical function were used to detect drug effects. Teachers, parents, and doctors all judged all three drug conditions superior to placebo with teachers preferring methylphenidate and parents haloperidol. These preferences were, however, smaller than differences between the drugs and placebo. Side effects though mild were much commoner in the high dose of haloperidol. Diagnosis did not appear to influence response to medication. In a related study, it is shown that while the low dose of haloperidol improved cognitive function, though to a lesser extent than methylphenidate, the high dose of haloperidol depressed it. There thus may be a conflict between the needs for social and behavioral control and the needs of the child for optimum cognitive function. This needs to be evaluated in the classroom where conditions are more demanding than in the laboratory and where cognitive effects may differ. Subject to this caution, haloperidol would seem to be a useful psychotropic drug in some children. 22 references. (Author abstract)

000928 Wolthuis, O. L. no address **Pharmacological substances influencing acquisition behavior in rats.** Medicina Psicosomatica (Roma). 20(4):375, 1975.

Results of a study indicating that piracetam enhances acquistion of a Y-maze and drink test task in rats were presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Analysis showed that enhanced acquisition was not due to effects of the drug on consolidation, retrieval or decay of information storage, neither was it the result of increased arousal or changed sensitivity to footshock. It is concluded that recent electrophysiological findings indicate that sensory function is not changed, i.e. the drug does not alter the electroretinogram. On the other hand, cortical responsiveness to stimulation of the eye with light flashes is significantly changed by the drug. The results suggest that the compound enhances acquisition by its effects on the first phase of information processing. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

000929 Allert, M.-L. Neurolog.-Psychiatr. Abteilung des ZentralKrankenhauses der Bundeswehr, Postfach 7460, 5400 Koblenz, West Germany /**Side-effects of psychotropic drugs.**/ Nebenwirkungen der Psychopharmaka. Medizinische Welt (Stuttgart). 27(11):512-516, 1976.

A review is presented of the treatment for the side-effects of prescribed psychotropic drugs. Situations requiring immediate treatment include: expansive states of arousal caused by neuroleptics, thymoleptics, and lithium salts; psychotic manifestations caused by neuroleptics and thymoleptics; dwindling of consciousness, sometimes to the point of coma, due to combined administration of psychotropic drugs; drug caused depression, with the possibility of compulsive suicide; hypertonic crisis caused by eating cheese while taking MAO-inhibitors; development of edema due to thymoleptics; acute extrapyramidal hyperkinesia produced by neuroleptics; epileptic

attacks and cardiac disorders caused by neuroleptics and antidepressants; atonia resulting from the use of diazepine derivatives. Noncrucial side-effects that the patient should be able to adjust to include Parkinsonism, restlessness, focusing problems, tachycardia, dry mouth, sweating, constipation, minor skin problems, sedation, and reduction of libido. Administering these drugs to children, adolescents and geriatric patients requires special restraint in determining dosage levels.

000930 Bafaqeeh, H. H.; Myers, D. H. Shrewsbury Hospital, Salop, England **Lithium and thyrotoxicosis.** The Lancet (London). I(7974):1409, 1976.

A letter reports a case of thyrotoxicosis in a patient on lithuim carbonate. The patient was a 50-year-old, manic-depressive who drank heavily. Daily doses of between 0.5and 1.0g of lithium carbonate had been used since 1971. But in April, 1974, his serum lithium reached 0.7mmol/1. He was then tremulous and fearful with sinus tachycardia of 144. Because of his heavy drinking it was thought he was developing delirium tremens. Two weeks later indications of thyrotoxicosis were confirmed. He had a score of 27 on the Wayne scale (a score of plus 19 suggests thyrotoxicosis). It is concluded that difficulties in the diagnosis resulted from the fact that hyperthyroidism poisons so many systems but none in a distinctive way and that lithium depresses the thyroid. 2 references.

000931 Bojdecki, Krzysztof. II Klinika Psychiatryczna, Instytutu Psychoneurologiczny, Warsaw, Poland **/Complications and side-effects in long-term treatment with practolol./** Powiklania objawy uboczne zwiazane z dlugotrwalym stosowaniem praktololu. Psychiatria Polska (Warszawa). 10(2):217-218, 1976.

Many side-effects have been observed following treatment with practolol, ranging from those affecting the vascular and respiratory systems, to disorders of the skin, sight, or hearing. In 100 psychiatric patients given 150-600mg no side-effects were observed. It is believed that such reported complications and side-effects arise only when dosage has been excessive. 10 references.

000932 Brandt, R. Abteilung fur Experimentelle Medizin der F. Hoffmann-La Roche & Co. AG, Basel, Switzerland **Passage of diazepam and desmethyldiazepam into breast milk.** Arzneimittel-Forschung (Aulendorf). 26(3):454-457, 1976.

The extent and nature of the passage of orally administered Valium into the breast milk of nursing mothers was studied. It was shown that diazepam and its main, active metabolite desmethyldiazepam passed into the milk. Their concentrations, however, remained small in comparison with plasma values. Desmethyldiazepam levels in the milk were consistently higher than diazepam levels. These results are due to the relative binding of both substances to plasma proteins. The maximum quantities of diazepam plus desmethyldiazepam that can possibly be absorbed by a newborn from the milk of a mother receiving 10mg Valium daily, are considered too small to cause any harmful effects in the baby. If, however, high doses of Valium must be administered repeatedly, breastfeeding should be discontinued for safety reasons. 10 references. (Author abstract modified)

000933 Brase, David A.; Loh, Horace H. Department of Pharmacology, University of California at San Francisco, San Francisco, CA 94143 **Comparison of the inhibition of 5-hydroxytryptamine uptake by methadone and its congeners in human platelets.** Biochemical Pharmacology (Oxford). 25(14):1684-1686, 1976.

The ability of methadone to appreciably inhibit uptake of 5-hydroxytryptamine (5-HT) by human platelets at concentrations likely to be encountered in methadone maintenance treatment was studied. Chlorimipramine, imipramine, dextro-methadone, levo-methadone, racemic methadone, dextro-alpha-methadol, levo-alpha-methadol, dextro-beta-methadol, levo-beta-methadol, dextro-alpha-acetylmethadol, levo-alpha-acetylmethadol, dextro-beta-acetylmethadol, levo-beta-acetyl-methadol, 1,5-dimethyl-3, 3-diphenyl-2-ethylidene pyrrolidine perchlorate, 3,3-diphenyl-2-ethyl-5-methyl-1-pyrrolidine hydrochloride and levo-alpha-nor-methadol hydrochloride were also tested for ability to inhibit 5-HT uptake by human platelets. All of the drugs and metabolites inhibit the uptake of 5-HT, with chlorimipramine being the most potent inhibitor. The compounds with the 6R configuration (levo-methadone, dextro-alpha-methadol, dextro-alpha-acetylmethadol, levo-beta-methadol, and levo-beta-acetylmethadol) are more potent uptake inhibitors than the compounds with the 6S configuration (dextro-methadone, levo-alpha-mehtadol, levo-alpha-acetylmethadol, dextro-beta-methadol and dextro-beta-acetyl-methadol). It is suggested that methadone is a more potent inhibitor of 5-HT uptake by platelets than was previously recognized, and the possibility exists that methadone maintenance therapy may result in depletion of platelet 5-HT. 17 references.

000934 Christensen, Hanne; Felby, Soren. Dept. of Forensic Medicine, Univ. of Copenhagen, Juliane Mariesvej 16, DK-2100 Copenhagen, Denmark **Dibenzepine and its metabolites in blood, muscle, liver, vitreous body and urine from fatal poisoning.** Acta Pharmacologica et Toxicologica (Kobenhavn). 37(5):393-401, 1975.

A separation technique followed by spectrophotometry for the quanitative determination of dibenzepine and its main metabolites in autopsy material is presented. The method, which has a lower detection limit of 0.5mu-g/g material, was used for blood, tissue and urine from 8 cases in which dibenzepine was considered to be the only or a contributory cause of death. In addition to unchanged dibenzepine, three N-demethylated metabolites were detected and identified in the material. According to the results the material could be divided into 2 groups. One group, 6 cases, with high concentrations total dibenzepine (dibenzepine plus metabolites), blood 23-147mu-g/g, liver 255-566mu-g/g in which death was caused by dibenzepine alone or in combination with alcohol, and another group, 2 cases, with 10 times lower total dibenzepine concentrations in blood and tissue; in this group additional factors might have contributed to death. 10 references. (Author abstract)

000935 Crowley, Thomas J.; Rutledge, Charles O.; Hoehn, Margaret M.; Stallings, Mary Ann; Sundell, Seymour. University of Colorado Medical Center, 4200 East Ninth Avenue, Denver, CO 80220 **Low urinary dopamine and prediction of phenothiazine-induced Parkinsonism: a preliminary report.** American Journal of Psychiatry. 133(6):703-706, 1976.

In order to test the hypothesis that those psychiatric patients with low urinary dopamine levels before treatment with antipsychotic drugs would be at greatest risk for developing parkinsonian side-effects following treatment, 16 patients were tested for dopamine excretion rate before being administered oral trifluoperazine and observed for development of extrapyramidal symptoms. Results indicated that psychiatric patients who excreted larger amounts of urinary free dopamine before treatment were significantly more likely than patients excreting smaller amounts to develop parkinsonian side-effects. It is suggested that urinary free dopamine determina-

tions could prove valuable in indicating which patients should receive those antipsychotic drugs least likely to produce extrapyramidal side-effects. 20 references. (Author abstract modified)

000936 Cubitt, Terence. Chase Wing, Enfield District Hospital, Enfield, Middlesex, ENZ 8FL, England **Lithium and thyrotoxicosis.** Lancet (London). 1(7971):1247-1248, 1976.

Thyrotoxicosis developed in a married woman of 59 who had received lithium carbonate for 16 months in treatment of cyclothymic personality disorder. Her psychiatric state was greatly improved, and administration of antacids, ferrous sulfate and carbimazole relieved the thyrotoxicosis associated anemia and tremor. It is suggested that lithium acts similarly to iodine, by direct inhibition of thyroid hormonal iodine release, resulting in a form of thyroid "escape".

000937 Degkwitz, R.; Consbruch, U.; Haddenbrock, S.; Neusch, B.; Oehlert, W.; Unsold, R. Psychiatrische und Nervenklinik, Hauptstrasse 5, D-7800 Freiburg i. Br., W. Germany **/Therapeutic risks in long-term treatment with neuroleptics and lithium./** Therpeutische Risiken bei der Langzeitbehandlung mit neuroleptika und Lithium. Nervenarzt (Berlin). 47(2):81-87, 1976.

Seventy patients treated for more than 10 to 12 years with neuroleptics were studied for possible negative side effects. The patients had received approximately one million neuroleptic quanta (dosage x potency), or about 1kg choloropromazine, 2kg thioridazine, or 300gm haloperidol. Liver function showed pathological gamma globulin values in 80% of the cases. Biopsy showed nonfestering cholangitis in 11 patients. The presence of eosinophilic granulocytes indicated an allergic process probably resulting from drug sensitivity. These findings show no essential therapeutic risk relative to liver function. Persistent extrapyramidal hyperkinesia was observed in 70% of the patients. The study showed that length of therapy was the most important factor contributing to side-effects. An additional group of 856 cases given lithium salts for more than 6 years was studied. Apparently 2/3 of the patients also received neuroleptics or thymoleptics, which means that the physicians did not rely solely on lithium. Side-effects were almost double in patients receiving the additional drugs. There was no indication that prophylactic effect was lessened when lithium was administered in doses regulated to avoid side-effects. 130 references. (Author abstract modified)

000938 Diehl, L. W. Psychiatrische Klinik der Freien Universitat Berlin, Nussbaumallee 36, D-1 Berlin 19, Germany **/Mental effects of antiepileptic drugs./** Psychische Wirkungen von Antiepileptika. Bibliotheca Psychiatrica (Basel). No. 151:190-200, 1975.

Direct and indirect psychotropic effects of antiepileptic drugs used singly and in combination are presented. Pharmaceuticals discussed include: primidone, phenobarbital, carbamazepine and diphenylhydantoin. The importance of optimizing each patient's drug therapy program is stressed. Complaints ascribed to drug effects by the patients include decreased mental performance, tiredness and impotence. More legitimate complaints may include disordered thought, limitation of attention span and reduced mental capacity in adults, and affection of memory, intelligence functions and learning capacity in children. 57 references.

000939 Donlon, P. T., Stenson, R. no address **Extrapyramidal symptoms with high dose neuroleptic agents. Incidence and management.** Medicina Psicosomatica (Roma). 20(4):392, 1975.

A study of the incidence, form, and response to contra-active therapy with 150 hospitalized patients receiving high dose neuroleptics (equivalent to 40 to 100mg/day fluphenazine) and not on prophylactic antiparkinsonian (AP) agents was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Clinical indications for administering AP agents in prevention and control of neuroleptic induced extrapyramidal symptoms (EPS) were discussed and the relationship between dose and EPS was outlined. (Author abstract modified)

000940 Dzialek, Ewa. Klinika Neurologiczna, Instytut Chorob Ukladu Nerwowego i Narzadow Zmyslow, AM, ul. Kopcinskiego 22, 90-153 Lodz, Poland **/Negative aspects of pharmacological prevention of epilepsy./** Ujemne aspekty farmakologicznego zapobiegania w padaczce. Neurologia i Neurochirurgia Polska (Warszawa). 10(2):191-195, 1976.

The neurotoxic effects of antiepileptic drugs often resulting in brain damage are discussed. Drug induced encephalopathy or neuropathy of this type occurs particularly in patients with liver diseases or enzyme deficiencies. Teratogenic and epileptogenic side-effects have been observed in cases treated with anticonvulsants. Conversely, several examples are given in which cranial trauma was followed by one or more epileptic seizures and characteristic EEG abnormalities, but despite absence of drug treatment, these patients have shown no seizures during the past several years and EEG has returned to normal. 32 references. (Author abstract modified)

000941 Ebranati, E.; Ridolo, P.; Chimini, R. II Ospedale Psichiatrico Provinciale di Brescia, Brescia, Italy **/Some notes on the patient with neuroleptic syndrome./** Alcune note sul vissuto del paziente che presenta la sindrome neurolettica. Rivista di Neuropsichiatria e Scienze Affini (Parma). 21(4):153-166, 1975.

Extrapyramidal side-effects of neuroleptic drugs are examined. An overview of the literature reveals that side-effects include changes in psychomotor functioning, altered body image, and anxiety and depression. It is concluded that any patient using neuroleptic drugs should be alerted to possible side-effects, as should his family. It is suggested that dosage be limited to the minimum needed to bring about the desired reaction, so as not to exacerbate the patient's condition. 46 references.

000942 Eggers, Christian. Abteilung fur Kinder- und Jugendpsychiatrie, Osianderstr. 14, D-7400 Tubingen, West Germany **/Toxicopathic hallucinatory syndromes in children./** Durch Vergiftungen hervorgerufene halluzinatorische Syndrome im Kindesalter. Neuropatologia Polska (Warszawa). 13(3-4):297-303, 1975.

The cause by chemical toxins of optical hallucinations in children in the absence of disorientation or unconsciousness is investigated. Seven children aged 2 to 9 had visions of animals, fairytale characters, and toys. The hallucinations lasted several hours to several days, and were accompanied by anxiety and agitation. The chemicals in question included tantum (a benzydamine derivative), atropine, hashish, fenfluramine (an anorexic), akineton, and an antihistamine (diphenylpyraline hydrochloride). It is presumed that toxic, hallucinogenic substances interfere with the filtering action of the thalamus, which protects the visuopsychic area of the cerebral cortex against irrelevant optical stimuli. Their underdeveloped capacity for differentiation between objective and subjective experience seems to make children particularly vulnerable to the neurophysiological effects of intoxication.

000943 Escande, M.; Gayral, L.; Goldberger, E.; Jarrige, A.; Kulik, J. Clinique Universitaire de Psychiatrie, Faculte de Medecine Purpan, Hopital de la Grave, F-31052 Toulouse, France **/Convulsive accidents and EEG modifications in the course of treatment by tricyclic antidepressants./** Accidents convulsifs et modifications E.E.G. au cours des traitements par les antidepresseurs tricycliques. Encephale (Paris). 2(2):133-151, 1976.

The effect of tricyclic drug treatment on the occurrence of convulsions and on the EEG is discussed. There is a review of the clinical and experimental literature. A total of 31 patients were studied who had an elevated risk of convulsions because of advanced age, previous convulsions, elevated dosage, or neurological problems. The patients are catagorized with regard to sex, age, diagnosis, antidepressant taken and dose, clinical observations, and EEG changes. The antidepressants used were imipramine, amitriptyline, and clomipramine. Only three patients had convulsions during antidepressant treatment; two of these had had electroshock therapy before the drug therapy. There was no correlation between clinical manifestations and EEG patterns. 17 references.

000944 Fann, William E.; Sullivan, John L.; Richman, Bruce W. Department of Psychiatry, Baylor College of Medicine, Houston, TX 77025 **Dyskinesias associated with tricyclic antidepressants.** British Journal of Psychiatry (London). 128:490-493, 1976.

Hyperkinetic movement disorders may occur as side-effects of antipsychotic drugs; and a hyperdopaminergic state induced by the neuroleptic compounds is thought to be a cause of extrapyramidal disorders such as tardive dyskinesia. Two cases of the dyskinetic syndrome in patients receiving tricyclic antidepressants (TCA) are discussed. Because the TCA are known to have little effect on striatal dopamine but do share with the neuroleptics potent anticholinergic activity, these cases appear to support the hypothesis that the drug induced hyperkinetic disorders are related to a diminution of CNS acetylcholine activity as well as to an increase in dopamine activity. (Author abstract modified)

000945 Feline, A.; Quetin, A.-M. No address **/Undesirable effect of beta-stimulant derivatives? Emergence of an acute psychiatric symptomatology in some mental patients./** Effet indesirable de derives beta-stimulants? Emergence d'une symptomatologie psychiatrique aigue chez des malades mentaux. Nouvelle Presse Medicale (Paris). 4(39):2808-2809, 1975.

Psychiatric decompensation in three women with psychiatric history and taking beta-adrenergic stimulants Duvadilan and Salbutamol is reported. All three women were pregnant. The symptoms of visual illusions, multisensorial hallucinations, and anxiety disappeared a few weeks after treatment was stopped. The observations are correlated with the fact that acebutolol, a beta-adrenergic blocking agent, acts on certain symptoms observed in chronic psychotics. The beta-adrenergic agents causing the psychiatric symptoms have structures comparable to those of other sympathomimetics such as amphetamines or mescaline.

000946 Fernandez, Peter G. Department of Medicine, Memorial University of Newfoundland, St. John's NF, Canada **Alpha methyldopa and forgetfulness.** Annals of Internal Medicine. 85(1):128, 1976.

Incidences of forgetfulness as an adverse effect of alpha-methyldopa used as a hypertensive agent in nine individuals is provided. Insufficiency of full documentation is noted. The incidences of forgetfulness as related to the addition of diuretics to alpha-methyldopa is cited, and the possibility of interaction of alpha-methyldopa, or its metabolites, or both, with diuretics is suggested. 3 references.

000947 Foerster, K. Neurolog. Klinik u. Poliklinik der Universitat Mainz, Langenbeckstr. 1, D-6500 Mainz, W. Germany **/Acute delirium syndrome in Addison's disease under cortisone substitution therapy./** Akutes delirantes Syndrom bei Morbus Addison unter Cortison-Substitutionstherapie. Nervenarzt (Berlin). 47(2):124-125, 1976.

A 32-year-old female patient exhibited acute delirium while under cortisone substitution therapy for Addison's disease (25mg prednisolone and 0.1mg fluorohydrocortisone/day). The possible causative factors considered included: 1) preexisting afebrile mild pharyngitis; 2) the stress situation of being confined to a clinical milieu; 3) a possible, but still undiagnosed protracted hypoglycemia. The diagnosis of delirium in Addison's disease appeared most probable. 10 references.

000948 Gisselmann, A.; Boudry, C.; Marin, A.; Ballivet, J. Service de Psychiatrie du C.H.U. de Dijon, Hopital General, 2, rue de l'Hopital, F-21033 Dijon, France **/Clinical and biochemical considerations on the depressive states supervening during parkinsonian syndromes treated by L-dopa./** Considerations cliniques et biochimiques sur les etats depressifs survenant lors de syndromes parkinsoniens traites par la L. Dopa. Encephale (Paris). 2(2):105-113, 1976.

Depression occuring in the course of parkinsonism treated by L-dopa is discussed. Of 116 patients treated, 17 developed depression. The depression could be classified as Type I (occurring at the onset of L-dopa therapy) or Type II (occurring later in the course of L-dopa therapy). The depressions could be subclassified according to whether or not they responded to tricyclic drugs. Hypotheses are offered as to the monoaminergic cause of the depression. 17 references.

000949 Goncalves, N.; Gruneberg, F. Psychiatrische Klinik der Freien Universitat Berlin, Nussbaumallee 36, 1 Berlin 19, West Germany **/Oral glucose tolerance test in schizophrenics under long-term neuroleptic treatment./** Einzeitige orale Glukosebelastung bei langfristig neuroleptisch behandelten Schizophrenen. Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 8(5):289-295, 1975.

The oral glucose tolerance test was carried out in 58 schizophrenic patients (45 females and 13 males) under long-term treatment with neuroleptics (41 receiving perazine, 10 clozapine and the remainder various other neuroleptics). Of this group 41 showed positive hyperglycemic reactions. Correspondences with different age groups could not be established. Because the values obtained from determining the fasting blood sugar are unreliable, the oral glucose tolerance test using 100g glucose is recommended as the routine procedure. Several hypotheses related to the action of neuroleptics on glucose metabolism are briefly discussed. Glucose tolerance tests and body weight controls should be conducted regularly during long-term neuroleptic treatment. 52 references. (Author abstract modified)

000950 Good, Michael I. Wes-Ros-Park Center, 1842 Centre Street, West Roxbury, MA 02132 **The concept of drug automatism.** American Journal of Psychiatry. 133(8):948-951, 1976.

The drug automatism hypothesis which implies a medication induced absence of intentionality for self-poisoning and a relative amnesia for serial or single overdosage is analyzed. Con-

troversy stems from problems encountered in the formulation and verification of the hypothesis. A case associated with a proprietary sleeping preparation is presented. Psychopharmacological and psychophysiological elements in the mechanism of drug automatism and its differential diagnosis are discussed. 24 references. (Author abstract modified)

000951 Gritz, Ellen R.; Shiffman, Saul M.; Jarvik, Murray E.; Schlesinger, Joseph; Charuvastra, V. C. Brentwood Veterans Administration Hospital 530/151D, Wilshire and Sawtelle Blvds., Los Angeles, CA 90073 **Naltrexone: physiological and psychological effects of single doses.** Clinical Pharmacology and Therapeutics. 19(6):773-776, 1976.

Physiological and psychological effects of dosage with the narcotic antagonist naltrexone were studied in human subjects. An ascending series of single doses of the drug, ranging from 20-160mg, was administered to 8 abstinent former addicts in order to assess agonistic activity and toxic side-effects. There was little alteration of normal body function in the subjects. Small changes in sublingual temperature (0.4degrees Fahrenheit decrease) and diastolic blood pressure (1.7mm Hg increase) were induced. Among the battery of tests assessing behavioral or mood feeling variables, two showed significant between condition effects (attention and perception, and mild euphoria). Subjects had few subjective reactions or unpleasant side-effects. It is concluded that naltrexone is a safe, nontoxic medication in the dosage range examined. 12 references. (Author abstract modified)

000952 Gruner, W. Horemer 9, D-74 Tubingen, Germany **/Exogenous psychosis in a patient with carcinoid syndrome following treatment with p-chlorophenylalanine./** Exogene Psychose eines Patienten mit Karzinoidsyndrom nach Behandlung mit p-Chlorophenylalanin (PCPA). Psychiatria Clinica (Basel). 8(5):266-276, 1975.

Case history of a patient with carcinoid syndrome who developed exogenous psychosis while under treatment with p-chlorophenylanine (PCPA) is reported. The patient exhibited symptoms similar to delirium and schizophrenia. A review of literature on PCPA shows that animals treated with PCPA develop avoidance and flight behavior, motor unrest, hypersexuality, aggressiveness, and convulsive depression. Significant phenomenological similarities were discovered between the patient's reactions and certain forms of amphetamine psychosis. The following biochemical mechanism is suggested to explain the origin of PCPA psychosis: reduction of cerebral serotonin caused by PCPA results in an increased noradrenaline turnover and eventual relative exhaustion of the noradrenaline supply. 22 references.

000953 Janssen, Folker. Univ.-Kinderklinik, Moorenstrasse 5, D-4000 Dusseldorf, West Germany. **/Disease caused by drug therapy in newborn infants./** Krankheiten durch Arzneimittel beim Neugeborenen. Monatsschrift fur Kinderheilkunde (Berlin) 123(1):34-37, 1975.

Withdrawal symptoms and other negative reactions to various drugs, including psychotropic drugs, are described in relation to newborn infants. Oversedated newborn infants exhibit deterioration of vital functions immediately upon or within a few minutes of severing the umbilical cord. A great drop in the APGAR number from the 1st to the 5th or 10th minute may indicate medication poisoning. In addition to these symptoms, diazepam results in severe temperature lability. Morphine withdrawal symptoms in newborn infants include motor restlessness, tremor, excessive sweating, sucking on the hands, vomiting, and diarrhea. Beginning 1 to 24 hours after birth 10% to 15% of infants whose mothers have been treated with reserpine for hypertension exhibit tachypnea and dyspnea, which can lead to cyanosis and feeding difficulties. Usually these symptoms diasppear spontaneously after a few days, but sometimes intubation is required. Continued research and education in the field of medication poisoning in the newborn is urgently required. 37 references.

000954 Johnson, Gordon F. S. Department of Psychiatry, Sydney Univeristy, Parramatta Road, Sydney, New South Wales 1006, Australia **Lithium neurotoxicity.** Australian and New Zealand Journal of Psychiatry (Carlton). 10(1):33-38, 1976.

Clinical changes that may occur as a result of lithium carbonate therapy are described and illustrated with case histories. The emergence of central nervous system toxicity is the most serious complication. The role that such factors as serum lithium levels, sodium balance, organic brain damage, clinical typology, concurrent physical illness, and drug interaction play in the genesis of this disorder is discussed. Permanent neurological damage following lithium poisoning is dependent of the duration and severity of neurotoxicity. Guidelines for appropriate use and monitoring of lithium in psychiatric disorders is suggested. 27 references. (Author abstract modified)

000955 Johnson, Rosemary A. Department of Pediatrics, Christchurch Hospital, Christchurch, New Zealand **Adverse neonatal reaction to maternal administration of intravenous chlormethiazole and diazoxide.** British Medical Journal (London). No. 6015:943, 1976.

Twelve of 14 women who had received both chlormethiazole and diazoxide during labor for treatment of preeclamptic toxemia gave birth to infants suffering from hypotonia, hypoventilation or apnea. A 13th infant with respiratory depression was born to a woman who had received chlormethiazole in addition to massive doses of anticonvulsants during labor. Chlormethiazole alone had not been reported to adversely effect infants born to women receiving the drug during labor. Adverse effects were not related to drug dosage or to the severity of maternal preeclamptic toxemia. Three infants died of the respiratory distress syndrome, the remainder were treated successfully via intermittent positive pressure ventilation. It is sugested that chlormethiazole and diazoxide act synergistically to produce respiratory problems in infants when the drugs are administered to their mothers during labor. 5 references.

000956 Kiely, William F. Department of Psychiatry, University of Southern California School of Medicine, 1200 N. State St., Los Angeles, CA 90033 **Psychiatric syndromes in critically ill patients.** Journal of the American Medical Association. 235(25):2759-2761, 1976.

An unanticipated dividend resulting from the spread of development of intensive care units in general hospitals has been the new respect developed by physicians, surgeons, and nurses for the mind/body interrelation in all illness. The integrative importance of the central nervous system has forced critical care unit personnel to appraise its functional state in ways comparable to their customary attention to cardiovascular, pulmonary, and renal functional indexes. Critical care psychiatric syndromes are seen to reflect multiple determinants reflective of personality characteristics, disease related factors, elements related to the intensive care unit's environmental impact, and medical/surgical treatment related features. Implications for therapy, with emphasis on appropriate use of psychoactive drugs, as well as on features in the environment itself that may be made more meaningful to the patient, are

emphasized in terms of their preventive and corrective value. 11 references. (Author abstract)

000957 Kunin, Richard A. 1030 Leavenworth Street, San Francisco, CA 94109 **The action of aspirin in preventing the niacin flush and its relevance to the antischizophrenic action of megadose niacin.** Journal of Orthomolecular Psychiatry. 5(2):89-100, 1976.

Biochemical pharmacaological action of niacin in treatment of schizophrenics is discussed in relation to the action of aspirin. Aspirin has been observed to block or attenuate the flush reaction caused by megadose niacin therapy in 90% of a group of schizophrenic and nonschizophrenic outpatients. The patients were not treated with tranquilizers or antiinflammatory agents concurrently. The basis for this phenomenon, the blocking of the niacin flush by aspirin, is hypothesized to be due to inhibition of prostaglandin synthesis by aspirin. In addition, inhibition of bradykinin by aspirin may also act to suppress the flush. The various components of the inflammatory system are described, and their relationship to the flush response is discussed. It is speculated that continued megadose niacin therapy leads to depletion of bradykinin and histamine and small increase in prostaglandins, particularly of the E type. These are known to exert an inhibitory effect on noradrenergic pathways and, along with the probability of reduced tissue histamine levels, produce an overall sedative effect. Thus niacin at megadose levels is often observed to act like a tranquilizer. This is suggested to account in part for the antischizophrenic action of megadose niacin therapy. 23 references. (Author abstract modified)

000958 Kunin, Richard A. 1030 Leavenworth Street, San Francisco, CA 94109 **Manganese and niacin in the treatment of drug-induced dyskinesias.** Journal of Orthomolecular Psychiatry. 5(1):4-27, 1976.

The use of manganese and niacin in treating drug induced withdrawal and tardive dyskinesia in 15 psychiatric patients is reported, and the frequency of occurrence and mechanisms of cause and treatment in such cases is discussed. All 15 subjects were treated with manganese chelate and 10 also received niacin or niacinamide. There were four cases (27 percent) of dramatic and almost immediate cure, after manganese treatment. In nine other cases (60 percent) definite improvement occurred in 2 to 5 days. In the one case unresponsive to manganese, niacin therapy was dramatically successful, associated with almost complete cure in a matter of hours. In eight of nine other cases in which niacin was used, it was associated with significant elevation of mood and clearing of sensorium. In seven of seven cases that also were treated with niacinamide, similar clearing of sensorium was noted and, in two cases, significant improvement in extrapyramidal symptoms. It is concluded that manganese appears to be of value in many cases of tardive and withdrawal dyskinesia, and that it also may be of value in preventing the occurrence of these side-effects. It is likely that niacin and niacinamide are of some value in many cases of drug induced extrapyramidal syndrome. More extensive and better controlled studies are needed to evaluate all of these observations and impressions. 55 references. (Author abstract modified)

000959 Lader, M. H. no address **Diazepam and aggression.** Practitioner (London). 216(1295):489-490, 1976.

The use of diazepam is questioned due to its association with occasional increased hostility and aggressive impulses. It is pointed out that, although rare, instances of diazepam's being implicated in increased aggression may indicate an alternative psychotherapeutic treatment. Oxazepam is suggested.

000960 Lakshminarayan, S.; Sahn, Steven A.; Hudson, Leonard D.; Weil, John V. Veterans Administration Hospital, 4435 Beacon Ave., So., Seattle, WA 98108 **Effect of diazepam on ventilatory responses.** Clinical Pharmacology and Therapeutics. 20(2):178-183, 1976.

To investigate the effects of diazepam on ventilatory control, hypoxic and hypercapnic ventilatory responses were studied in eight normal subjects before and after 10mg of intramuscular diazepam. There was no significant change in either resting minute ventilation or resting end tidal CO2 tension, but depression of hypoxic ventilatroy response was observed 15 (60% of control) and 30 min (53% of control) after diazepam. No significant depression of hypercapnic ventilatory response was noted 70 to 130 min after diazepam. In view of the depression of hypoxic ventilatory response by diazepam in normal subjects, adverse responses along these lines should be considered in patients with impaired ventilatory function, such as chronic airways obstruction, and in those encountering acute hypoxemia. 28 reference. (Author abstract)

000961 Lambert, P.-A.; Dachary, J.-M.; Marie, C.; Oules, J.; Pagot, R.; Sales, M.; Vauterin, C. Clinique de Bressieux, Hopital de Bassens, Chambery (Savoie), France /**A new synthetic antiparkinson agent, tropatepine hydrochloride, in extrapyramidal syndromes induced by neuroleptics.**/ Un nouvel antiparkinsonien de synthese le chlorhydrate de tropatepine dans les syndromes extrapyramidaux induits par les neuroleptiques. Encephale (Paris). 2(2):115-121, 1976.

Tropatepine HCl, a new antiparkinsonian agent, was studied in 218 patients. Of these, 184 patients, 121 males and 63 females, ranging in age from 19 to 85, received the drug orally. All were inpatients at the beginning of the study and were receiving major tranquilizers. The mean dose of tropatepine was 18mg/day, and the mean length of treatment was 37 days, with a range of 3 days to more than 6 months. Improvement was noted in akinesia in 82% of 132 patients, in hypertonia in 86.6% of 143 patients, in tremor in 75% of 129 patients, in chronic hyperkinesia in 70% of 73 patients, and in hypersialorrhea in 70% of 38 patients. The drug was also effective in early dystonic crises and oculogyric crises. Tropatepine was active and well tolerated in two patients with senile parkinsonism. Maximal efficacy of tropatepine occurs on the fifth or sixth day of treatment. In an open study with 140 patients and in a double-blind study with 96 patients comparing tropatepine with trihexyphenidyl, the two drugs were judged to be equivalent. Side-effects of tropatepine included dry mouth, difficulty in accommodation, mydriasis, asthenia, and somnolence. No changes in laboratory tests, EEG, cardiac findings, or ocular findings were noted. In 34 patients, tropatepine was given parenterally in a dose of 10 to 20mg/day, and the same results were obtained as by oral administration. No habituation was reported. 16 references.

000962 Lin, James T-Y.; Ziegler, Dewey, K. Department of Neurology, University of Kansas Medical Center, Rainbow Blvd. at 39th St., Kansas City, KS 66103 **Psychiatric symptoms with initiation of carbidopa-levodopa treatment.** Neurology. 26(7):699-700, 1976.

Psychoses developed in two patients after their antiparkinsonism medication was changed from levodopa alone to a combination of levodopa and carbidopa. The combination therapy was instituted in both cases after an appropriate levodopa free period. Despite adherence to the appropriate and recommended dosage, the first patient developed hallucinations, agitation, and then manic psychotic behavior, with hypersexuality and violence necessitating physical restraint.

After a withdrawal period, treatment with levodopa alone was resumed and the psychiatric symptoms disappeared. The second patient became agitated, delusional and withdrawn; hallucinations and marked emotional lability developed. Carbidopa was withdrawn and treatment with levodopa alone resumed. The psychiatric manifestations subsided; however, periodic disorientation and emotional lability persisted. It is suggested that the brief period of levodopa withdrawal prior to institution of the combination therapy may result in a lowerng of the drug requirement so that resumption of therapy with levodopa and carbidopa subsequently results in the psychiatric manifestations occasionally associated with overdosage. 6 references.

000963 Lingjaerde, Odd. Department of Clinical Psychiatry, University of Tromso, Tromso, Norway **Effect of doxepin on uptake and efflux of serotonin in human blood patelets.** Psychopharmacology (Berlin). 47(2):183-186, 1976.

It is shown that the tricyclic antidepressant drug doxepin (comprising 15% of the cis-isomer and 85% of the trans-isomer) is a moderately potent competitive inhibitor of serotonin uptake in human blood platelets in vitro. The inhibitory effect was 6 times stronger in an artificial, protein free medium than in diluted plasma, corresponding to about 85% protein binding. The efflux of serotonin from platelets preloaded with 14C-serotonin was not affected by doxepin in concentrations up to 10 to the minus 6M, but increased rapidly at concentrations above 10 to the minus 4M. It is difficult to say whether therapeutic dosages of doxepin have an inhibitory effect on the 'serotonin pump' strong enough to exert a significant inhibitory effect on this pumping mechanism in serotoninergic neurons. However, Fann et al. found that doxepin in a daily dosage of 200-300mg in depressed patients reduced the platelet serotonin content; this reduction is probably due to uptake inhibition, and doxepin thus seems at least to have an in vivo effect on the serotoninergic system in platelets. 14 references. (Author abstract modified)

000964 Lingsch, C.; Martin, K. Department of Pharmacology, University of Cambridge, Hills Road Cambridge CB2 2QD, England **An irreversible effect of lithium administration to patients.** British Journal of Pharmacology (Basingstoke). 57(3):323-327, 1976.

The inhibition of choline uptake into erythrocytes that is associated with lithium therapy was studied in order to determine whether this effect is truly irreversible or a consequence of the presence of lithium inside the cells. Lithium administration to patients results in a pronounced inhibition (about 90%) of the choline transport system in erythrocytes. The transport system does not recover when the erythrocytes are treated to remove intracellular as well as extracellular lithium. When lithium therapy is discontinued, the choline transport system of the patients' red blood cells recovers very slowly over a period of 3 months, i. e.,at about the same rate at which the erythrocytes that had been exposed to lithium are replaced by new cells. It is concluded that therapeutic concentrations of lithium produce an irreversible inhibition of the choline transport system in human erythrocytes. Because erythrocytes do not metabolize choline, this effect is probably of no consequence; however, the problem remains of determining whether this possibly species specific inhibition of choline transport occurs in other tissues, especially the central nervous system. 9 references. (Author abstract modified)

000965 MacLennan, William. Dept. of Geriatric Medicine, University of Southampton, Southampton, England **/Drugs which create problems for the elderly./** Dangerous drugs. Nursing Times (London). 72(28):xii, 1976.

Drugs which can prove to be dangerous for the elderly are discussed. Agents which normally induce drowsiness or sleep often produce frank confusion in the elderly. These include the barbiturates, Mandrax (methaqualone and diphenhydramine hydrochloride), most of the anti-Parkinsonian drugs, methyldopa and, surprisingly, digoxin. Increasing age may also impair the ability of the brain to control blood pressure, and thus, the elderly are particularly sensitive to drugs which have an effect on the autonomic nervous system. These drugs include many hypotensive agents, antidepressants, anti-Parkinsonian drugs, and atropine and its substitutes. The elderly are also sensitive to diuretics which lower blood volume. The sensitivity of the hypothalamus is reduced in old age and it is readily suppressed by agents which act as sedatives. These include the barbiturates and the phenothiazine tranquilizers. Diabetes is particularly common in the elderly and drugs which upset glucose metabolism (steroids and many of the widely used diuretics) can produce side-effects.

000966 Mann, J. I.; Doll, Richard; Thorogood, Margaret; Vessey, M. P.; Waters, W. E. Department of Social and Community Medicine, University of Oxford, Oxford, England **Risk factors for myocardial infarction in young women.** British Journal of Preventive and Social Medicine (London). 30(2):94-100, 1976.

Seventy seven women discharged from the hospital with a diagnosis of myocardial infarction and 207 women control patients, all under 45 years of age, were compared in order to determine the risk factors associated with myocardial infarction. Oral contraceptives, which have previously been implicated as a risk factor in this age group, were not considered in this study. Heavy cigarette smoking, reported treatment for preeclamptic toxemia, and type II hyperlipoproteinemia are independent risk factors for myocardial infarction. Reported treatment for hypertension and diabetes are probably also independently associated with subsequent development of the condition. The association between myocardial infarction and reported treatment for obesity appears to be secondary. An association between myocardial infarction and previous treatment for a psychiatric complaint was found. The increased risk was greatly reduced after standardization for other factors, suggesting that the association is secondary rather than causal. It is suggested that an association between personality type and the development of myocardial infarction may exist, or that some of the drugs used to treat these complaints may be involved. Alternatively, nonspecific symptoms occurring before an acute myocardial infarction may result in patients being treated for such symptoms by psychotropic drugs. Examination of the effect of several factors combined suggests that they act synergistically, as the presence of three or more factors increase the risk 128 fold. 15 references. (Author abstract modified)

000967 Mariani, Fidel H. A. Universidad de Buenos Aires, Buenos Aires, Argentina **/Chronic use of marijuana./** Intoxicacion cronica por marihuana. Neuropsiquiatria (Buenos Aires). 6(4):202-215, 1975.

The various works of many authors and researchers on the long-term effects of chronic use of marijuana was studied. Many writers maintain that prolonged use results in symptoms such as disturbance in affective reactions, indifference to the environment, irresponsibility, impulsive actions lacking motivation, loss of memory and attention, slow reactions, various changes in intelligence, hallucinations, restlessness, and

depression. Other researchers refute these results, saying that they saw only a decrease in inhibition, increase in self-confidence and freedom from anxiety. Other possible destructive effects of prolonged use include arterial lesions, possible deforming effects on fetus, effect on immunization system, and respiratory functions. 95 references.

000968 Mendelson, Wallace B.; Deza, Plaridel C. Laboratory of Clinical Psychopharmacology, St. Elizabeth's Hospital, NIMH, Washington, DC **Polydipsia, hyponatremia, and seizures in psychotic patients.** Journal of Nervous and Mental Disease. 162(2):140-143, 1976.

Case histories are presented for four psychotic patients who ingested large quantities of water and subsequently developed grand mal seizures and serum sodium levels of less than 121meq/liter. The physiology of psychogenic polydipsia, hyponatremia and related disorders are reviewed. It is speculated that temporal lobe seizures may be related to excessive drinking behavior in some cases and that psychiatric patients on phenothiazines may be more susceptible to seizures from hyponatremia than other patients. 12 references. (Author abstract modified)

000969 Mikkelsen, Bent; Birket-Smith, Erik; Brandt, Sven; Holm, Per; Lund, Mogens; Thorn, Ingrid; Vestermark, Svein; Olsen, Poul Zander. Department of Neurology, Hjorring Hospital, DK-9800 Hjorring, Denmark **Clonazepam in the treatment of epilepsy: a controlled clinical trial in simple absences, bilateral massive epileptic myoclonus, and atonic seizures.** Archives of Neurology. 33(5):322-325, 1976.

The effects of the combined use of clonazepam and previously administered antiepileptic drugs were compared with the effects of placebo combined with the same antiepileptic drugs in patients who had not responded satisfactorily to previous medication. The antiepileptic effect of clonazepam was significantly superior to placebo. Side effects of somnolence, fatigue, drowsiness, and coordination disturbances occurred in most patients, but subsided spontaneously or could be controlled by slow increase or slight reduction of dosage. Mental side-effects such as agitation, confusion, and aggressiveness were more troublesome and caused discontinuation of clonazepam in two patients. 15 references. (Author abstract modified)

000970 Miyazaki, Yuji. Department of Neurological Surgery, Sapparo Medical College and Hospital, Sapparo, Japan **On the effect of dopa decarboxylase inhibitor for the Parkinson's disease patients treated by L-dopa for long term.** Brain and Nerve (Tokyo). 27(6):621-628, 1975.

Patients suffering from Parkinson's disease (N=70) were treated with L-dopa and on a long-term basis experienced various decreased therapeutic effects, "on and off" phenomena relating to efficacy of dosage and certain side-effects. These side-effects included: gastrointestinal symptoms, headaches, and psychiatric disorders such as depression and hallucinations. Six patients treated with a combined therapy of L-dopa and MK-486 in a fixed ratio (10:1) experienced relief from gastrointestinal problems, and reduced psychiatric side-effects. The combined therapy also restored the efficacy of the original L-dopa dosage. 30 references. (Author abstract modified)

000971 Muller-Oerlinghausen, B. Psychiatrische Klinik der Freien Universitat, Nussbaumallee 36, D-1000 Berlin 19, Germany **/Avoiding undesirable physical side-effects during therapy with psychotropic drugs./** Zur Vermeidung unerwunschter korperlicher Nebenwirkungen bei der Therapie mit Psychopharmaka. Nervenarzt (Berlin). 47(3):211, 1976.

Caution is urged in the administration of supplementary therapy drugs such as cholinesterase inhibitors or beta-receptor blockers to counteract arrhythmic side-effects of certain antidepressants as recommended in two previous articles in "Nervenarzt." A study by the Boston Collaborative Drug Surveillance Program recently revealed the great danger of even small doses of propranolol, a beta-receptor blocker, in possibly causing serious side-effects. Patients should be advised by their physicians about the therapeutic purpose and possible side-effects of beta-blockers and thereby reach an informed decision about the use of such drugs. Physicians should avoid routinely administering combinations of drugs unless the therapeutic situation shows an actual need.

000972 Myers, E. D.; Calvert, E. J. St. Edward's Hospital, Staffordshire, England **The effect of forewarning on the occurrence of side-effects and discontinuance of medication in patients on dothiepin.** Journal of International Medical Research (Northampton). 4(4):237-240, 1976.

The effect of doctors' forewarning of side effects on their occurrence and on subsequent discontinuance of medication was investigated. Dothiepin was prescribed for 100 depressed outpatients alternately allocated to one of two groups. Patients in Group A were forewarned about side-effects and patients in Group B were not forewarned. None of the patients had previously received dothiepin. After two weeks the patients were questioned regarding side-effects and continuance with medication. Eighty nine patients were included in the final analysis. The results failed to confirm the hypotheses that forewarning patients of side-effects causes a greater number of patients to complain of such effects, or that where patients experience side-effects, forewarning is associated with any less frequent discontinuance of therapy. Compared with a previous study with amitriptyline, the results of this study are much closer to statistical significance. This may be due to the lower overall incidence of side-effects with dothiepin; therefore, further work with a larger sample of patients is recommended. 9 references. (Journal abstract modified)

000973 Nesse, Randolph; Carroll, Bernard J. Neuropsychiatric Institute, University of Michigan Medical Center, University Hospital, Ann Arbor, MI 48104 **Cholinergic side-effects associated with deanol.** Lancet (London). 2(7975):50, 1976.

A letter reports a serious occurrence in one patient of cholinergic side-effects associated with deanol (2-dimethylamino-ethanol). A patient, a 37-year-old woman, with tardine dyskinesia of 4 years, had not responded to other drugs. Symptoms included oral, lingual, buccal movements that caused teeth and tongue biting. After 17 days of 1500mg deanol per day, she complained of dyspnoea and respiratory difficulty. Examination disclosed rhinorrhea, sialorrhea, but no infection. Deanol was discontinued, and within 16 hours, the symptoms improved. In 2 days the rhinorrhea and sialorrhea had stopped. The letter concludes that deanol, useful in the management of some learning disorders and hyperkinesis in childhood, may act in man by conversion to choline and acetylcholine. 3 references.

000974 no author. no address **Alcohol-drug interactions in daily medical practice.** Practical Psychology for Physicians. 3(7):35-36, 1976.

A chart is presented in which the classes of drugs which may with alcohol (analgesics, anesthetics, antialcohol preparations, antianginal drugs, antidiabetic drugs, antihistamines, antihypertensive agents, anticoagulants, anticonvulsants, antidepressants, antiinfective agents, central nervous system stimulants, diuretics, sedative hypnotics, tranquilizers, and vitamins) are listed. The possible effects and clinical significance of the interactions are presented.

000975 Parent, M. Clinique Psychiatrique, Universite de Liege, Liege, Belgium **/Secondary effects of psychotropic drugs./** Effets seconds des psychotropes. Revue Medicale de Liege (Liege). 31(7):241-244, 1976.

The side-effects of tranquilizers and antidepressants are reviewed. Hypnotic drugs may cause dependence with abstinence symptoms on withdrawal. The barbiturates cause interaction when given with a number of other medications. The minor tranquilizers may cause somnolence and are potentiated by alcohol. Withdrawal after administration of large doses may cause abstinence symtpoms. Side effects of the major tranquilizers are sedation, hypotension, extrapyramidal symptoms, amenorrhea, and galactorrhea. There is a brief discussion of irreversible extrapyramidal symptoms. The CNS stimulants cause irritability, insomnia, anxiety, depression, dependence, anorexia, hypertension, and psychiatric syndromes. MAO inhibitors cause hypotension, confusion , and impotence. They should not be given concomitantly with another class of antidepressants, with alcohol, or with foods such as fermented cheeses, spinach, herring, anchovies, yeast, or bananas. Side-effects of the tricyclic drugs are anticholinergic effects, anxiety and sedation. 10 references.

000976 Pfeifer, Henry J.; Greenblatt, David J.; Koch-Weser, Jan. Boston Collaborative Drug Surveillance Program, 400 Totten Pond Road, Waltham, MA 02154 **Clinical toxicity of reserpine in hospitalized patients: a report from the Boston Collaborative Drug Surveillance Program.** American Journal of the Medical Sciences. 271(3):269-276, 1976.

Adverse reactions to reserpine were studied in 231 hospitalized medical patients who received the drug. Reserpine was administered specifically for hypertension in 91.3% of patients; 35.5% of patients received the drug by intramuscular (IM) injection. The IM route of administration was associated with higher mean daily doses than was oral administration. Adverse reactions to reserpine were reported in 26 patients (11.3%), but only three of these reactions were considered life-threatening, and no deaths were attributed to the drug. Central nervous system (CNS) disturbances, reported in 12 patients, were the most common unwanted effects. Gastrointestinal disturbances were reported in six patients, and hypotension in six. Toxicity occurred more frequently in those who received rauwolfia derivatives prior to admission; however, this group of patients also received IM reserpine more frequently. Finally, reserpine toxicity, in particular CNS disturbances, was reported more frequently in patients also receiving barbiturates, suggesting additive CNS effects. 39 references. (Author abstract)

000977 Pouget, R.; Blayac, J.-P.; Largey, B.; Alric, R.; Castelnau, D.; Boulet, J. Clinique universitarie de Psychiatrie Adulte, C.H.U., Montpellier, France **/Corneal and lens lesions caused by treatment with neuroleptics of the phenotiazine type./** Depots corneens et cristalliniens dus aux traitements par neuroleptiques de type phenothizine. Annales Medico-Psychologiques (Paris). 1(3):403-407, 1976.

To investigate a possible correlation between treatment with neuroleptics and corneal or lens lesions, 186 hospitalized patients were studied. Out of this number, 39 had not been treated with phenothiazine and presented no ocular disorders. Among the remaining 147 patients treated with phenothiazines, 35 (24%) presented ocular lesions. It was concluded that the ocular lesions were caused by the phenothiazines, and the total quantity of phenothiazines absorbed was a good measure of ocular toxicity. This paper was presented at the Feburary 1976 meeting of the French Medical Psychology Association. 10 references.

000978 Presley, A. P.; Kahn, A.; Williamson N. General Hospital, Steelhouse Lane, Birmingham B4 6NH, England **Antinuclear antibodies in patients on lithium carbonate.** British Medical Journal (London). No.6030:280-281, 1976.

Fifty patients who had been taking lithium carbonate for periods of 2 months to 10 years underwent blood estimation of antinuclear factor (ANF). Test results were compared to those of a control group of 50 patients matched for age, sex and disease. ANF was estimated using standard immunofluorescence technique and other antitissue antibodies were observed. The majority of patients tested were suffering from psychotic depression or manic-depressive psychosis. None of the controls were positive for ANF, while of the test group 11 were positive for ANF. Findings indicate an 18% incidence in patients receiving lithium, while the absence of DNA antibodies in the ANF positive patients indicates they did not have true systemic lupus erythematosus. 5 references.

000979 Prusek, Wieslaw; Radomska, Grazyna; Winiewicz, Zdzislaw. Oddzial Dzieciecy Wojewodzkiego Szpitala Zespolonego, Plac 1 Maja 8, 50-043 Wroclaw, Poland **/Accidental Benalgin poisoning./** Wypadkowe zatrucie Benalginem. Wiadomosci Lekarskie (Warszawa). 28(12):1091-1092, 1975.

A 2-1/2-year-old male was hospitalized for accidental poisoning caused by ingestion of 8 tablets (4,000mg) of Benalgin (Benzydamine, a nonsteroidal anti-inflammatory drug). The patient developed severe agitation, tonic/clonic seizures, and occasional loss of consciousness. Upon regaining consciousness hallucinations developed in which the patient claimed he was being attacked by a very large frog. After gastric lavage his behavior returned to normal. Review of a number of similar cases tends to confirm that in toxic doses Benzydamine is hallucinogenic. 13 references. (Author abstract modified)

000980 Reid, William H.; Blouin, Paule. 1121 Paseo de Peratta, Santa Fe, NM 87501 **Outpatient psychiatric medications and glaucoma.** Psychosomatics. 17(2):83-85, 1976.

The possible precipitation or exacerbation of glaucoma as a result of the administration of commonly used psychotropic medications was studied. Fifty outpatients who were taking a variety of psychotropic drugs in a variety of dosages were the study subjects. No glaucomatous side effects were detected. 35 references.

000981 Reilly, T. M. Department of Psychological Medicine, Middlesex Hospital, Mortimer Street, London W.1, England **Physiological dependence on, and symptoms of withdrawal from, chlormethiazole.** British Journal of Psychiatry (London). 128:375-378, 1976.

The uses of chlormethiazole (Heminevrin), chiefly a central nervous system depressant with an early onset of sedative/hypnotic effect, are briefly outlined. Differing views of its potential for producing dependence are discussed. The consen-

sus opinion is taken to be that a risk of psychological dependence does exist, but only one case has appeared in the medical literature to date of physiological dependence on chlormethiazole, with withdrawal symptoms. This case is reexamined. A second case is described in which the features of increasing dosage and withdrawal were followed by confusion, disorientation, delusions, hallucinations and muscular spasm and coarse jerking. This is taken as confirmation of the potential of chlormethiazole to produce physiological dependence. Some personal opinions of the author regarding indications for use and incidence of the drug's abuse are briefly mentioned. 11 references. (Author abstract modified)

000982 Riordan, Charles E.; Mezritz, Marjorie; Slobetz, Frank; Kleber, Herbert D. Clinical Research Unit, 106 Park Street, New Haven, CT 06519 **Successful detoxification from methadone maintenance: follow-up study of 38 patients.** Journal of the American Medical Association. 235(24):2604-2607, 1976.

A followup study of 38 patients attempting detoxification from methadone maintenance after heroin addiction is reported. Thirty eight patients were successfully detoxified from maintenance with methadone hydrochloride. Contrary to results of most previous studies, a substantial number of individuals were found to have remained drug free, employed, and uninvolved with the criminal justice system since detoxification. Almost half of those who returned to drug use have become reinvolved in treatment. Escalated alcohol use occurred during and following methadone maintenance. The alcohol consumption of detoxified (from methadone) patients is seen as a problem in continued successful rehabilitative outcome. The followup study is being continued to ascertain long-term outcome of patients detoxified from methadone maintenance. 6 references. (Journal abstract modified)

000983 Segelman, Alvin B.; Segelman, Florence P.; Karliner, Jerrold; Sofia, Duane. College of Pharmacy, Department of Pharmacognosy, Rutgers University, Busch Campus, New Brunswick, NJ 08903 **Sassafras and herb tea: potential health hazards.** Journal of the American Medical Association. 236(5):477, 1976.

Preliminary phamacological experiments have shown that certain aqueous and alcoholic extracts prepared from sassafras root bark can elicit a variety of pharmacological reponses in mice. These responses include taxia, ptosis, hypersentivity to touch, central nervous system depression, and hypothermia. Safrole is also a potent inhibitor of certain liver microsomal hydroxylating systems, a property that could cause toxicity if drugs metabolized by these enzymes are administered together with sassafras tea. The potential health hazard of sassafras and other herb teas is suggested especially in concomitant use with drugs which are prescribed. It is suggested that physicians evaluate their patients in terms of extemporaneous herb tea usage (discouraging the practices usually) when use of other drugs is required for therapy. 13 references.

000984 Siegel, Ronald K. Department of Pharmacology, UCLA School of Medicine, Los Angles, CA 90024 **Herbal intoxication: psychoactive effects from herbal cigarettes, tea, and capsules.** Journal of the American Medical Association. 236(5):473-476, 1976.

Psychoactive effects from herbal cigarettes, tea, and capsules are reported. The herbal preparations, designed to be smoked or ingested for reasons of health and happiness, are promoted as legal hallucinogens, euphoriants, and marihuana substitutes. A total of 25 such substances are identified in these products, and a number of intoxications have been reported from their short-term or long-term use. Physicians are alerted to the nature of these effects when taking drug histories in order to consider their possible role in the causation of medical complaints. The psychoactive substances which are known include African yohimbe bark (yohimbe), broom (Scotch broom), California popy, catnip, cinnamon, damiana, hops, hydrangea, juniper, kavakava, kola nut (Gotu kola), lobelia, mandrake, mate, Mormon tea, nutmeg, passion flower, periwinkle, prickly poppy, snakeroot, thorn apple, tobacco, valerian, wild lettuce, and wormwood. Reported effects of these substances include mild or strong hallucinations, strong sedation, hypnotism, euphorism, stimulation, narcotism, analgesia, and tranquilization. 16 references. (Journal abstract modified)

000985 Simpson, G. M.; Branchey, M. H.; Lee, J. H.; Voitashevsky, A.; Zoubok, B. Rockland Research Institute, Orangeburg, NY 10962 **Lithium in tardive dyskinesia.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(2):76-80, 1976.

In a study of the effect of lithium on tardive dyskinesia two tests were performed. A single-blind pilot study of 10 patients, 2 males and 8 females 50 to 85 years old, mean age 71 years, and mean hospitalization 20 years (range: 3 to 38 years) with tardive dyskinesia resulting from long-term neuroleptic therapy failed to show any beneficial effects of lithium administration. Because regular neuroleptic medication had been continued throughout this study, a double-blind trial of lithium and placebo with suspension of regular neuroleptic therapy was done in three males and seven females, primarily schizophrenics, 57 to 82 years of age (mean age 72 years), hospitalized 9 to 43 years (mean hospitalization 30 years). Results showed essentially no change in the dyskinetic symptoms over the trial period. The severity of the symptoms fluctuated from week to week, but this was not related to the treatment. Although the results of both studies were negative, the resistance to lithium treatment may have been due to the severity and chronicity of the symptoms, which may account for reported successes in early onset of tardive symptoms. 11 references.

000986 Simpson, Lance L. Department of Pharmacology, College of Physicians and Surgeons, Columbia University, 630 W. 168th St., New York, NY 10032 **The effect of behavioral stimulant doses of amphetamine on blood pressure.** Archives of General Psychiatry. 33(6):691-695, 1976.

The ability of amphetamine to produce sustained increases in blood pressure was studied in humans and in rats. Blood pressure was monitored in 14 patients who sought medical attention for an adverse behavioral reaction to self-administered amphetamine. There is no evidence that amphetamine evokes a sustained increase in blood pressure in these patients. Determination of the doses of amphetamine that cause behavioral stimulation and an evaluation of the blood pressure effects of the same doses of amphetamine was performed in rats. In control animals, behavioral stimulant doses of amphetamine exert only transient effects on blood pressure. In pithed animals, i.e. animals devoid of all central mechanisms, amphetamine exerts a sustained effect on blood pressure. It is concluded that the potential ability of amphetamine to evoke sustained cardiovascular responses is suppressed via baroreceptor reflexes and perhaps other central regulatory mechanisms in intact animals. 16 references. (Author abstract modified)

000987 Steiner, J.; Cassar, J.; Mashiter, K.; Dawes, I.; Fraser, T. Russell; Breckenridge, A. University of Kanses,

Medical Centre, Kansas 66103 **Effect of methyldopa on prolactin and growth hormone.** British Medical Journal (London). 1(6019):1186-1188, 1976.

The effects of administration of methyldopa on serum prolactin and growth hormone (GH) concentrations in hypertensive patients were studied. Single doses of methyldopa (750 or 1000mg) significantly increased serum prolactin levels, peak concentrations occurring 4 to 6 hours after drug administration. Long-term methyldopa treatment was associated with threefold to fourfold increases in basal prolactin levels compared with those in normal subjects. In patients treated with methyldopa for 2 to 3 weeks the GH response to insulin was significantly greater than in normal subjects and untreated hypertensive patients. In contrast, patients treated for prolonged periods (mean 13.4months) had a GH response indistinguishable from normal. 18 references. (Author abstract modified)

000988 Struve, Frederick A.; Saraf, Kishore R.; Arko, Robert S.; Klein, Donald F.; Becka, Dorothy R. Hillside Hospital, 75-59 263rd St., Glen Oaks, NY 11004 **Electroencephalographic correlates of oral contraceptive use in psychiatric patients.** Archives of General Psychiatry. 33(6):741-745, 1976.

An investigation was carried out to determine whether measuring electroencephalogram (EEG) during sleep would show additional EEG/oral contraceptive relationships not previously suspected on the basis of measuring EEG during wakefulness. With blind procedures, EEG data and oral contraceptive use data were obtained from 110 women. Three age equated comparison groups were formed: 1) women who had never used oral contraceptives; 2) had previously used oral contraceptives with side-effects; and 3) had previously used oral contraceptives without side-effects. A significant statistical relationship exists between paroxysmal EEGs and occurrence of side-effects during oral contraceptive use. No difference in paroxysmal EEG incidence is reported between women not taking oral contraceptives and those experiencing no side-effects during use of oral contraceptives. Among prior pill users, women with paroxysmal EEGs report having had almost twice as many side-effects as do women with normal EEGs. It is suggested that the hypothesis of West and West (1966), that oral contraceptive use may aggravate or exacerbate preexisting cerebral dysrhythmias resulting in symptomatic developments not previously experienced at all or at least not strongly displayed, may interpret these results. Attention is called to the importance of drowsiness and sleep activation in studies of this nature. The majority of the EEG findings depended on such recording conditions and would have been missed if only waking studies had been done. 34 references. (Author abstract modified)

000989 Trimble, M. R.; Reynolds, E. H. Department of Neurology, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8 AF, England **Anticonvulsant drugs and mental symptoms: a review.** Psychological Medicine (London). 6(2):169-178, 1976.

Since the effects of anticonvulsant drugs on the mental processes of epileptic patients are suggested to be adverse, these effects should be more clearly defined. Comparative tests are needed between the conventional anticonvulsant drugs such as phenobarbitone, DPH and primidone and newer anticonvulsant drugs. The effects of a single drug as opposed to multiple drugs also need assessment. Other drugs utilized in neuropsychiatric illness should also be considered suspect. Chronic phenothiazine therapy has been implicated in permanent dyskinesia, and other psychotropic drugs used in long-term treatment may also be adversely affecting the patient's intellectual processes due to neglect of sufficient research. 62 references.

000990 Tuchmann-Duplessis, H. Laboratoire d'Embryolgie, Faculte de Medicine de Paris, Paris, France **Monographs on Drugs. Vol. II.** Acton, MA, Publishing Sciences Group, 1975. 267 p. $15.00

The factors, pharmacological and otherwise, that may have dysmorphogenic effects on the embryo and fetus are described. Among the topics discussed are prenatal physiology, embryonic nutrition, and the principal mechanisms of teratogenic action. Although most of the information indicating drugs as having adverse effects on a fetus was obtained in laboratory animal experiments, obvious effort is made to extrapolate the significance of these animal studies to clinical medicine. Each section, whether it relates to drugs, vaccines, metabolic disorders, or radiation damage, includes information on the likely risk to the human fetus of the suspected teratogens described.

000991 Volden, G. no address **Neurotoxicity associated with sulphones.** Acta Dermatovener (Stockholm). 56(1):77, 1976.

A case of peripheral neuropathy associated with use of sulphones is presented. A 60-year-old man with a typical dermatitis herpetiformis had been taking sulphapyridine once or twice daily from 1948-1956, when he became tired and weak, and suffered from tinnitus and cyanosis of the lips. When given aldesulphone sodium 0.666-1.3g daily, his condition improved rapidly. In 1968, numbness and a tingling feeling in toes and fingertips occurred and gradually spread proximally. This was treated with diaphenylsulphone 100-125mg daily until 1972. The paresthesia intensified and spread to knees and elbows, with a feeling of coldness, but no subjective strength loss. The patient became psychologically unbalanced. He stopped taking sulphones in 1972 and took prednisone 10-25mg daily. The paresthesia disappeared and his psychological condition improved, but the skin disease remained active. He was hospitalized in 1975 and tested with diaphenylsulphone 150mg daily and a gluten free diet. He developed distal symmetrical paresthesia after 2 days, his nails turning brown and his lips becoming cyanosed. When the dose was reduced to 50mg daily, paresthesia gradually abated and when medication stopped, it completely disappeared in 3 days. This and other reports suggest that neurotoxicity of sulphones is dose related. (Journal abstract)

000992 von Lieven, Th.; Dietz, V.; Schulte, P. W. Karlstrasse 6, D-8900 Augsburg, Germany **/Pharmacogenic chronic hallucinosis: a case of chronic hallucinosis in late life after long-term treatment with psycholeptics./** Pharmakogen ausgeloste chronische Halluzinose: ein Fall einer chronischen Halluzinose im hoheren Lebensalter nach langdauernder Einnahme von Psycholeptika. Nervenarzt (Berlin). 47(3):176-178, 1976.

The case history of a 69-year-old female patient is reported who exhibited chronic visual and auditory hallucinosis after taking psycholeptics over a period of 10 years for chronic, hypochondriacally tinted depression with refractory sleep disorders. When the medication was suspended the hallucinosis gradually subsided. Reinstatement of the psycholeptic was followed by reappearance of the hallucinatory phenomena. It is suggested that administration of the psycholeptic created a mild psychological syndrome localized in the brain, which favored the appearance of the hallucinatory syndrome. 11 references. (Author abstract modified)

000993 Wallace, Sheila J. no address **Phenobarbitone for convulsions in children.** British Medical Journal (London). 1(6019):1213-1214, 1976.

In reply to a statement questioning the justification of the prescription of phenobarbital for convulsions in children, it is stated that no difference has been noted between treated patients and untreated patients in learning behavior or intellect. Epileptic children receiving phenobarbital achieve more educationally and have fewer behavior problems than other epileptic children not receiving phenobarbital. No significant reduction is noted in the Wechsler Intelligence Scale for children in children receiving phenobarbital for at least 1 year prior to the age of 7 years. A reduced verbal quotient is related to the recurrence of convulsions. It is suggested that longer, better controlled studies are needed before barbiturates are discarded in favor of less frequently used and possibly more harmful anticonvulsants. 11 references.

000994 Whyte, S. F.; MacDonald, A. J.; Naylor, G. J.; Moody, J. P. Dept. of Psychological Medicine, University of Glasglow, Glasglow, Scotland **Plasma concentrations of protriptyline and clinical effects in depressed women.** British Journal of Psychiatry (London). 128:384-390, 1976.

A study is presented which sought to find the relationship between side-effects, clinical outcome and the drug plasma levels in 28 female depressed patients treated with protriptyline. After 24 days of treatment, patients with plasma levels within a median range (630 to 900nmol/l) showed better responses to the drug than patients with plasma levels outside this range. There were no statistically significant correlations between plasma levels and side-effect scores or corrected side-effect scores (scores after subtracting pretreatment values) for the group at any time after starting the treatment. But positive correlations between plasma levels and corrected side-effect scores for the neurotic subgroup after 14 and 21 days of treatment were found. Other correlations between plasma levels and side-effect scores were nonsignificant. 20 references. (Author abstract modified)

000995 Wilson, John T. Department of Pediatrics, Vanderbilt University, Nashville, TN 37215 **Special problems for drugs used in children.** Southern Medical Journal. 69(6):779-786, 1976.

The relative lack of prescribing information for physicians to determine dosage levels for pediatric drug therapy is demonstrated by several case studies of overdose reactions to drugs such as aspirin, diphenylhydantoin, primidone and diazepam. Some drugs in use for many years – acetyl salicylic acid, diphenylhydantoin, and primidone – have disposition characteristics which lead to new uses (loading dose for DPH) or to unexpected toxicity (ASA, DPH, primidone). Prolonged use in many children of different ages does not imply understanding of metabolism or precise dose requirements. Diazepam, though unapproved in injectable form for children under 12-years-old, has been used widely in infants and older children in this country and abroad. Much yet needs to be known about its dose and plasma levels associated with clinical effect or toxicity in the child and neonate. Analytical capability can and should be applied to define drug absorption, distribution and elimination in children so that rational dosage guidelines can be developed for both new and old drugs. 98 references.

000996 Winstead, Daniel K. no address **Hiccups following ingestion of oral chlordiazepoxide.** American Journal of Psychiatry. 133(6):719, 1976.

In a letter to the editor, a patient treated for anxiety is reported to have developed hiccups after each ingestion of chlordiazepoxide. This side-effect for oral dosages of this benzodiazepine is unreported elsewhere. 1 reference.

000997 Wittenborn, J. R.; Flaherty, Charles F., Jr.; Hamilton, Leonard W.; Schiffman, H. Richard; McGough, W. Edward. Rutgers University, New Brunswick, NJ 08903 **The effect of minor tranquilizers on psychomotor performance.** Psychopharmacology (Berlin). 47(3):281-286, 1976.

The effects on a limited spectrum of psychomotor functions of a standard daily regimen of chlordiazepoxide, prazepam and placebo were studied in a three way double-blind comparison in normal volunteers. A learning effect was conspicuous for all drugs on all criteria during the sequence of 10 trials. For the most part the differences between the drug groups were insignificant, but there were distinctive modifications in the performance of the chlordiazepoxide group. The clearest effect of medications was found in time estimation tests. Paradoxically the drugs correct a naturally occurring perceptual error. Although it is not clear that the changes observed with administration of 10mg chlordiazepoxide three times daily present an impairment and a threat to safety, it is stated that the findings should not be generalized to the cumulative effects of continued medication or to the immediate effects or cumulative effects of high dose levels. 18 references. (Author abstract modified)

000998 Wren, James, C; Dana, Jacob B. Veterans Administration Center, Togus, ME 04330 **Electrocardiographic changes during lithium therapy.** Journal of the Maine Medical Association. 67(7):185-189, 1976.

Electrocardiographic changes were monitored during the first 4 weeks of treatment with lithium (38 patients) or placebo (40 patients) in 78 chronic alcohoic patients. The incidence of lowering and altered contours of the T-waves was significantly higher among the lithium treated subjects. Only one electrocardiogram was reported as borderline and none was interpreted as abnormal during the observation period. It is suggested that electrocardiographic changes due to lithium are usually benign. 13 references. (Author abstract modified)

000999 Zakrzewska, Franciszka. Instytut Psychoneurologiczny, Sobieskiego 1/9, 02-957 Warsaw, Poland /**Effect of trihexiphenidil on excitability of plantar flexor alpha motor neurons in drug induced parkinsonian rigidity.**/ Wplyw triheksyfenidylu na pobudliwosc motoneuronow alfa miesnia zginacza podeszwowego stopy w polekowej sztywnosci parkinsonowskiej. Neurologia i Neurochirurgia Polska (Warszawa). 9(1):15-24, 1975.

The effect of trihexiphenidil on the excitability state of alpha motor neurons of the plantar muscle in patients with drug induced parkinsonian rigidity and on the excitability of motor neurons of soleus muscle was assessed. Subjects were 12 psychiatric patients of a control group that received no medication, 13 similar patients treated with chlorpromazine, and 12 patients receiving phenothiazine compounds with a piperazine ring on the side chain. Excitability was tested 30 to 50 min after oral administration of 5mg trihexiphenidil. Results showed trihexiphenidil raised excitability to an extent dependent upon the original state of the muscle, with especially good results obtained when the plantar flexor muscle was determined by stimulation of the afferent fibers of the soleus muscle. 14 references. (Journal abstract modified)

001000 Zakrzewska, Franciszka. Instytut Psychoneurologiczny, Sobieskiego 1/9, 02-957, Warszawa, Poland /**Curve of excitability of alpha motor neurons of the dorsal flexor of the foot in drug induced parkinsonian rigidity before and after administration of ethylbenzatropine.**/ Krzywa pobudliwosci motoneuronow alfa miesnia zginacza grzbietowego stopy w polekowej sztywnosci parkinsonowskiej przed i po podaniu etylobenzoatropiny. Neurologia i Neurochirurgia Polska (Warszawa). 9(1):25-35, 1975.

The state of excitability of motor neurons of the dorsal flexor of the foot was evaluated in patients with drug induced muscle rigidity of the anterior tibial muscle. Subjects were 10 patients receiving chlorpromazine therapy and 10 patients not receiving psychotropic drugs. At periods of 30 to 50 min after administration of 5mg ethylbenzatropine i.m. the muscle excitability curves were tested. Results showed that ethylbenzatropine apparently has no effect on the excitability of motor neurons in the dorsal flexor muscle of the foot when tested by conditioned afferent stimulation. 12 references. (Journal abstract modified)

001001 Zingraff, J.; Jungers, P.; Drueke, T.; Man, N. K.; Crosnier, J. no address /**Accidental lithium poisoning in a chronically hemodialyzed patient.**/ Intoxication accidentelle par le lithium chez un hemodialyse chronique. Nouvelle Presse Medicale (Paris). 4(45):3183-3185, 1975.

A case report of accidental lithium poisoning in a 54-year-old patient with chronic renal insufficiency who was on hemodialysis 3 times a week is presented. The patient had depressive tendencies and was receiving 25mg per day amitriptyline. He was given lithium carbonate by error instead of aluminum hydroxide. Symptoms were digestive problems on the second day, extrapyramidal hypertonia on the fourth day, and coma with tremor, myoclonia, and respiratory problems on the eighth day. At that time, lithium level in the blood was 3.0mEq per unit and in the cerebrospinal fluid, 1.1mEq per unit. The patient was successfully treated with hemodialysis and recovered; however, a hyperreflexia and a positive left Babinski sign remained. There was a delay of 4 to 8 days between the beginning of lithium ingestion and the onset of signs of toxicity. 19 references.

16 METHODS DEVELOPMENT

001002 Biggs, John T.; Chang, Sidney S.; Sherman, William R.; Holland, William H. Dept. of Psychiatry, Washington University School of Medicine, 4940 Audubon Ave., St. Louis, MO 63110 **Measurement of tricyclic antidepressant levels in an outpatient clinic.** Journal of Nervous and Mental Disease. 162(2):46-51, 1976.

A research project was undertaken to determine if the measurement of tricyclic antidepressant plasma levels provides a rational approach to improve clinical management of the depressed patient. Data were collected to determine if the routine measurement of plasma tricyclic antidepressant levels was practical in a large clinic population, and to determine if such levels could improve patient care. Individual differences in drug metabolism and frequent unreliable ingestion of medication make the measurement of drug plasma levels the only sure means of determining if a patient is receiving a fair therapeutic trial on a particular tricyclic antidepressant. Plasma analysis revealed both the failure to ingest adequate amounts of medication as prescribed and also the abuse of medications. It was concluded that generalizations regarding individual variation in drug metabolism or concerning drug compliance do little to improve patient care. When such problems are met on an individual basis, it is believed that many clinical management problems can be resolved. 13 references. (Author abstract modified)

001003 Curry, Stephen H. Dept. of Pharmacology and Therapeutics, London Medical College, Turner Street, London E1 2AD, England **Gas-chromatographic methods for the study of chlorpromazine and some of its metabolites in human plasma.** Psychopharmacology Communications. 2(1):1-15, 1976.

Gas chromatographic methods for the study of chlorpromazine presently in use at the London Hospital Medical College are presented along with comments on various alternatives available. The techniques are applicable to cerebrospinal fluid, urine and plasma but are not recommended for whole blood. Procedures are given for extraction and assay of chlorpromazine and its analogs and derivatives. Incorporation of 0.1% isovaleraldehyde into the toluene reagent is recommended to improve the separation effectiveness. The methods assess both protein bound and free drug (or metabolite) in human plasma, since the solvents effectively remove all reversibly bound phenothiazine molecules from protein surfaces. Results are compared with previous similar studies in the literature. 28 references.

001004 de Carvalho, Dermeval; Prado, Baptista Aymar; Larini, Lourival. Faculdade de Farmacia e Odontologia de Ribeirao Preto, Universidade de Sao Paulo, Rua Tibirica, 714, 14.100 Ribeirao Preto, SP, Brazil /**The use of spot tests as a means of identifying phenothiazine derivatives in emergency cases.**/ O emprego da analise de toque como meio de identificacao de derivados fenotiazinicos em casos de urgencia. Revista Brasileira de Medicina (Rio de Janiero). 32(5):314-316, 1975.

A rapid spot test to identify 12 phenothiazine derivatives, which can be useful, even lifesaving in emergency cases, is described. Three colorimetric reagents are used: 1) potassium dichromate, 2) potassium permanganate/cobalt nitrate, and 3) platinum chlorida/potassium iodide. An analytic scheme indicating the colors developed by a reagent or by successive treatment of a sample with two of the reagents is diagrammed, along with the identity of the derivatives corresponding to these colors. Results on samples in 0.2N hydrochloric acid agreed with results on samples extracted from urine by a standard rapid extraction method. 13 references.

001005 Heimann, Hans. Psychiatrische Universitatsklinik, D-7400 Tubingen, Germany /**Methodological problems in clinical trials of psychotropic drugs.**/ Methodologische Probleme bei der Effizienzprufung von Psychopharmaka. Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 220(3):255-268, 1975.

Methodological problems in developing differential efficacy profiles within the major psychotropic drug groups are generally discussed. Two aspects of the testing method are discussed: 1) problems in rating pathological behavior and longitudinal improvement in pathological behavior and 2) problems in selecting sample groups of psychiatric patients. Three groups of physicians (specialists in internal medicine, general practitioners and psychiatrists) were compared on the basis of their ability to rate the effects of a minor tranquilizer versus a placebo. The internists and the general practitioners were unable to differentiate between the two groups because of inexperience in observation. The psychiatrists were able to recognize the effectiveness of the minor tranquilizer. Main problems in selecting samples are discussed including the loss of information essential for recognizing finer differences in

drug effects resulting from taking the mean of a group of psychiatric patients; the important role of biological rhythms, which is too often neglected in clinical studies; based on case studies of two depressive patients, the enormous difference in psychophysiological responsiveness that can be hidden behind two similar clinical pictures. Only experiments involving a much greater display of individual symptoms which take into account all aspects of observation of selected single cases and longitudinal studies can help differentiate the subtle effects of psychotropic drugs and determine which drug within a major group is specifically appropriate for an individual patient. Psychophysiological and biochemical methods should be given priority over other methods. 14 references.

001006 Kobayashi, Kenichi. Tokyo Metropolitan Matsuzawa Hospital, Tokyo, Japan **Pharmacotherapy.** In: Hamada, S., Psychiatric treatment and nursing. Tokyo, Nippon Kango Kyokai Shuppan-kai, 1975. (p. 413-436).

The history, types, and effects of the use of psychotropic drugs for mental illness are reviewed. Therapeutic drugs are categorized and listed as: 1) tricyclic antidepressants (imipramine, chloroimipramine, despramine, primimine); 2) monoamine oxidase inhibitors (phenelzine, isocarboxazid); 3) psychological stimulants (methamphetamine, pipradol, methylphenidate); 4) major tranquilizers (phenothiazine, butyrophenone, reserpine); and 5) antianxiety drugs (meprobamate, chlordiazepoxide, hydroxyzine, chlormezanone). Effects of the drugs and their side-effects are outlined, and statistics are presented which show the limits and the effect ratios for all psychotropic drugs. These are compared on a yearly basis to show a gradual upturn in the effectiveness of drug treatment.

001007 Lawn, D. no address **A tight psychotherapeutical framework for the discussion of the effects of psychopharmaca.** Medicina Psicosomatica (Roma). 20(4):430, 1975.

A tight psychotherapeutical framework for evaluation of effects of psychotropic drugs was presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975). Several therapeutic dimensions were integrated into a tight interrelationship incorporating dimensions of client centered therapy, the A-B scale of Whitehorn and Betz, and a dimension arising from Janov's levels of consciousness hypothesis. The "holes" of Gestalt therapy possibly appear naturally, and a representation of multiple personality is also possible. Vectors and integrals possibly measurable in the "tree space" should correlate with psychological parameters. It was concluded that movement among the three personality dimensions of the framework offers a simple three space for discussion of the effects of psychotropic drugs. (Author abstract modified)

001008 Marholin, David, II; Phillips, David. Department of Special Education, Boston University, 765 Commonwealth Ave., Boston, MA 02215 **Methodological issues in psychopharmacological research: chlorpromazine -- a case in point.** American Journal of Orthopsychiatry. 46(3):477-495, 1976.

The methodology employed in evaluating the therapeutic efficacy of chlorpromazine (CPZ) is critically examined because of questions raised about its mechanism of action, possible interference with previous learning, transfer from drug state to nondrug state, and physical side-effects. Past studies are evaluated with regard to the following research design criteria: 1) placebo control; 2) random assignment of subjects; 3) use of double-blind technique; 4) standardized dosages; 5) standardized evaluations; and 6) appropriate statistical analyses. For the most part these studies have relied on group designs which may mask critical individual differences in drug responses. A research strategy employing within subject designs using a single subject as his own control is suggested as advantageous in assessing individual drug effects at specific dosage levels. 98 references.

001009 O'Brien, J. E.; Hinsvark, O. N. Analytical Chemistry Department, Pharmaceutical Division, Pennwalt Corporation, Rochester, NY 14623 **GLC determination of doxepin plasma levels.** Journal of Pharmaceutical Sciences. 65(7):1068-1069, 1976.

A procedure is described for extracting deoxepin, a tricyclic antidepressant, from plasma and subsequently measuring its concentration by GLC. The developed technique permits the resolution and quantitative determination of the cis isomer and trans-isomer of doxepin as well as its desmethyl metabolite. The method allows precise, reliable measurement of the drug and one of its metabolites in concentrations as low as 10ng/ml of plasma. 3 references. (Author abstract)

001010 Parent, M. no address **/Clinical parameters of antidepressant activity./** Parametres cliniques de l'activite antidepressive. Feuillets Psychiatriques de Liege (Liege). 8(4):447-459, 1975.

Clinical parameters of the activity of antidepressants are examined. Three essential components constitute the global antidepressant effect of a thymoanaleptic: the hormic, psychotonic and anxiolytic effect. Secondary effects of antidepressants due to their psychotropic activity are described. To explain existing differences between the predictions of pharmacology and activity in clinical experiences, problems related to semantic divergence and posological modifications are examined. The relationship between plasma level and antidepressant dosage is also explored. Graphic representations of the activity of antidepressants are included. 10 references.

17 MISCELLANEOUS

001011 Ablad, Bengt; Borg, Karl Olof; Carlsson, Enar; Ek, Lars; Johnsson, Gillis; Malmfors, Torbjorn; Regardh, Carl-Gunnar. Research Laboratories, AB Hassle, Fack, S-431 20 Molndal, Sweden **A survey of the pharmacological properties of metoprolol in animals and man.** Acta pharmacologica et Toxicologica (Kobenhavn). 36(5):7-23, 1975.

Results of toxicological and general pharmacological studies in the dog, the rat, mice and man indicate that metoprolol is a highly specific beta-blocker which has preventive antihypertensive action. The effect is associated with impaired vasoconstrictor fiber control. Pharmacokinetic studies indicate that metoprolol is completely absorbed after oral administration. First pass elimination in man is about 55% and independent of dose in the therapeutic dose range. Metoprolol is eliminated from human blood plasma with a half-life of 3 to 4 hours. The main metabolites were isolated and characterized pharmacologically. Unchanged metoprolol appears to be responsible for the beta-blocking action. 63 references. (Author abstract modified)

001012 Addabbo, A. Ospedale Psichiatrico S. Niccolo, Siena, Italy **/Observations on the use of psychopharmacology in psychiatric hospitals./** Alcune considerazioni sull'uso dello psicofarmaco in ospedale psichiatrico. Rassegna di Studi Psichiatrici (Siena). 65(2):355-364, 1976.

The role and value of psychopharmacology in psychiatric hospitals is discussed in the light of such factors as the ideology and methodology behind psychiatry, the economic interests, and the meaning of remission with psychotropic drugs in societal and medical contexts. It is concluded that psychopharmacology should not be used as a social tranquilizer, rather it should principally support the psychiatric treatment in question. 34 references.

001013 Audisio, M.; Pisarz, A.; Lemercier, C.; Pellenc, M.; Vervisch, A.; Lepoetre, M. Service de Sante Mentale de la Vallee de la Seine, 4, rue Paul-Eluard, F-76301 Sotteville-les-Rouen, France **/1035 MD (Sureptil) a cerebral vasoregulator and neuropsychotropic agent: results after ten years of use in psychiatry./** Le 1035 MD (Sureptil) vasoregulateur cerebral et neuropsychotrope: bilan apres dix annees d'utilisation en psychiatrie. Psychologie Medicale (Paris). 8(2):311-318, 1976.

The pharmacology of Sureptil is discussed. Sureptil is a combination of heptaminol and cinnarizine. Cinnarizine is a coronary dilator and heptaminol increases blood pressure; together the 2 constituents potentiate each other, correcting the vasodepressant effect of the psychotropic agents. Sureptil is also a major tranquilizer and by improving the cerebral circulation improves the diffusion of other medications. Thus it can be used to potentiate the effects of all psychotropic agents. Sureptil also appears to have a direct effect on neuronal functioning. The drug is particularly useful in alcoholic psychoses and mental retardation, as well as in pregnancy and geriatrics. 28 references.

001014 Axelrod, Julius. Section on Pharmacology, Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, MD 20014 **Central catecholamine neurotransmitters and psychoactive drugs (unpublished paper).** NIMH, 5600 Fishers Lane, Bethesda, MD, 1976. 20 p.

The interaction between catecholamine neurotransmitters (noradrenaline, dopamine and adrenaline) and drugs which affect behavior, is discussed. The origin of catecholamine nerve tracts within specific areas of the brain, the structures through which they pass, the structures innervated by their terminals, and the relative concentrations of the neurotransmitters within the various brain structures are described. The biosynthesis, metabolism, storage, release, inactivation by reuptake into nerve terminals and actions at postsynaptic receptors of the transmitters are described. Examples of psychoactive drugs which act on each of these functions to produce their behavioral effects are given, and the mechanism by which the drugs act on these functions is described. 37 references.

001015 Bar, Jurg. St. Gallen, Switzerland **/The advance of depressive diseases./** Vormarsch der depressiven Krankheiten. Praktische Psychiatrie (Zurich). 54(10):286-288, 1975.

A cost use analysis of antidepressants in Switzerland produced some statistics suitable for estimating future epidemiology of depression. The annual incidence of new cases of depression in Switzerland is 220,000, which is more than 3.5% of the total population. The number of prescriptions for antidepressants is between 500,000 to 600,000 per year, more than 90% of which are dispensed outside of hospitals. The incidence of psychogenic depression will increase considerably in comparison with the growth rate of the general population, endogenous depressions will remain stable, and the incidence of somatogenic depression will increase slightly. The occurrence of depression will increase an average of about 7% per year to 1995. The total antidepressants sold in Switzerland in 1972 cost 12 million SF. The estimated cost for 1995, including doctor visits, will be 62 million SF. In 1950, 40% to 60% of patients suffering from depression were treated with electroshock. By 1960 this was reduced to 10% because fo the introduction of antidepressants. In 1972, electroshock therapy cost 940 SF, compared to 30 SF for an equivalent 6 week course of antidepressant therapy. It is estimated that approximately 220,000 depressive patients are 33% more productive now due to chemotherapy. The total working days saved for depressive patients by chemotherapy in 1995 will produce an increase of 370 million SF in the gross national product.

001016 Beckmann, H. Psychiatrische Klinik der Univ., Nussbaumstrasse 7, 8000 Munich 2, West Germany **/Use and abuse of psychotropic drugs./** Gebrauch und Missbrauch von Psychopharmaka. Medizinische Welt (Stuttgart). 27(11):523-527, 1976.

The widespread abuse of psychotropic drugs, typical abusers, and the resultant strain on the physician-patient relationship is examined. General practitioners, especially, tend to overprescribe sedatives and stimulants. Psychiatrists and neurologists follow close behind general practitioners and internists in prescribing psychotropic drugs. Doctors are pressured, particularly by women and patients over 40, to provide long-term prescriptions for tranquilizers. This tendency holds true in England, also, where patients usually are unable to use the threat of changing doctors as a pressure tactic. Women patients in England who seek to obtain tranquilizers regularly usually have histories of early marriage, early divorce, few friends, poor social contact, and an extremely reserved attitude towards all personal contact. Women make up 2/3 of all tranquilizer consumers, and are 3 times as likely as men to become addicted to amphetamine stimulants or tranquilizers of the benzodiazepine group. Increased drug consumption is due

to such social factors as greater demands for efficient job performance, the stress of overpopulation, mass transit, and the information explosion. 11 references.

001017 Berger, Frank M. 190 E. 72nd Street, New York, NY 10021 **Present status of clinical psychopharmacology.** Clinical Pharmacology and Therapeutics. 19(6):725-731, 1976.

Topics discussed in a review of the present status of clinical psychopharmacology include: the psychotropic drugs (antipsychotics, antidepressants, and anxiolytics) with respect to treatment indications, treatment results, and clinical and research implications of use of such drugs. It is concluded that contributions of psychopharmacology do not rest solely on the therapeutic efficacy of the psychotropic drugs. The drugs in research and clinical application have stimulated new knowledge and areas of research in neurophysiology, psychiatry, and behavioral sciences, especially with regard to correlating biochemical aberrations with pathology and symptoms. It is suggested that better differential diagnosis between patients suffering from intrinsic mental disease and those patients who are disintegrating mentally under stress would be useful in developing improved therapy for both groups of individuals. 36 references.

001018 Bohme, K.; Dittbrenner, M. Psychiatrische Klinik, Vossstrasse 4, D-6900 Heidelberg, Germany **/Means and methods used in suicide attempts./** Mittel und Methoden bei Selbstmordversuchen. Nervenarzt (Berlin). 47(3):201-208, 1976.

Between 1947 and 1968, 2937 patients were treated at the Psychiatric and Neurological Clinic of the Medical School in Lubeck, West Germany for attempted suicide. The 3514 different means and methods used in these attempts are discussed. During this period 68% of these suicides were attempted with prescription drugs. Various poisons played only a minor role, mechanical means showed no increase and alcohol was rarely used as the main method. In relation to fatalities and acute clinical presentation the most dangerous methods were poisons, gas, prescription drugs and other means. Hypnotics and sedatives were used in 45.7% of cases, analgesics and other drugs in 18% and psychopharmacological drugs in 4.1%. In the use of psychopharmacological drugs, females accounted for 70.1% and males 29.9% of cases. The psychological and psychiatric therapy and prophylaxis of suicidality are discussed. Because of the absolute increase in suicidal use of drugs, greater caution is advised in their prescription, with an eye to screening possible suicide candidates. In addition to followup psychiatric care, initiated as soon as possible after hospital release, it is suggested crisis intervention centers be expanded for suicide prevention. 18 references.

001019 Brewer, Colin. University Department of Psychiatry, Queen Elizabeth Hospital, Birmingham, England **Suicide with tricyclic antidepressants.** British Medical Journal (London). No.6027:110, 1976.

The increasing and disproportionate share of deaths from suicidal poisoning attributable to tricyclic antidepressants is discussed. An increase in such suicides is cited in terms of the percentage of suicides and also in absolute numbers. It is suggested that manufacturers of such drugs include precautionary statements in their advertising. 3 references.

001020 Bridenbaugh, R. Harlan. Washington, DC **/Prescriptive guidance for usage of psychopharmaceuticals./** Practicing what we preach. American Journal of Psychiatry. 133(6):717-718, 1976.

Questions are raised in a letter to the editor to define the sources of prescriptive guidance on which psychiatrists should depend in choosing psychopharmacological treatments for their patients. Is the physician taking a malpractice risk by prescribing for indications other than those in the PDR and approved by FDA? If he so prescribes, should he inform his patient? Is he taking a malpractice risk if he prescribes on the basis of ignoring current literature which has not been approved by FDA? The illustration is presented that lithium, although not approved by FDA in unipolar depression treatment, has been proven conclusively to prevent recurrence of manic-depressive illness. 1 references.

001021 Brimblecome, R. W.; Pinder, R. M. no address **Hallucinogenic agents.** John Wright, 1975. 288 p. L12.50.

The major classes of hallucinogens are reviewed. Topics discussed range from the plants of South America to the structure of the amphetamines and the toxic effects of LSD.

001022 Browne, Thomas R. Seizure Unit, Children's Hospital Medical Center, 300 Longwood Avenue, Boston, MA 02115 **Clonazepam: a review of a new anticonvulsant drug.** Archives of Neurology. 33(5):326-332, 1976.

The anticonvulsant effects, toxicity, and clinical pharmacology of clonazepam, a benzodiazepine derivative, are presented. The drug is approved for treatment of typical absence, infantile myoclonic, atypical absence, myoclonic seizures, and akinetic seizures. The drug is rapidly absorbed the oral route and passes quickly from blood to brain. Preliminary results indicate a biological half life of 22 to 32 hours and a therapeutic serum concentration of 5ng/ml to 50nl/nml. Many studies report tolerance to the anticonvulsant effects with chronic administration. Major side-effects are drowsiness, ataxia, and behavior changes. They tend to be dose related, occur early in the course of therapy, and may subside with chronic administration. The dosage is begun at a low level and increased slowly. 81 references. (Author abstract modified)

001023 Burner, M. Centre Psycho-Social, Saint-Pierre 1, CH-1003 Lausanne, Switzerland **/Man's use of drugs through the ages./** L'homme face aux medicaments. Psychologie Medicale (Paris). 8(2):279-290, 1976.

A brief history of man's use of drugs is presented. In the papyrus of Ebers, which is more than 3,500 years old, 700 medicinal substances with their indications are listed. Two of the drugs included are morphine and opium. The use of opium from Homer to the 19th century is reviewed. The historic and scientific evolution of drugs has shown five periods since 1800: the first medical accomplishments of chemistry, the discovery of the hypodermic injection, the introduction of synthetic products, the birth of specific chemotherapy, and the introduction of tranquilizers. The prevalence of self-medication and of prescription writing is discussed. The action of medications may be a purely pharmacodynamic effect, a purely psychological effect, or a combination of both. The placebo effect may be a positive effect or a negative effect, or there may be no placebo effect. The action of a medication depends upon both the attitude of the physician and the attitude of the patient. 12 references.

001024 Caille, E.-J.; Bassano, J.-L. Centre d'etudes et de Recherches de Psychologie Appliquee, F-83800 Toulon, France **/A study of the protective properties of Segolan in hypoxia./** Etude des proprietes protectrices du Segolan dans une hypoxie. Psychologie Medicale (Paris). 8(2):321-331, 1976.

Segolan (ethane sulfonate of dihydroergotoxine) was administered to six adults ranging in age from 25-years-old to 40-years-old in a dose of 15mg. All subjects also received placebo under double-blind conditions. Two conditions were used for both active drug and placebo -- inhalation of air at a normal oxygen pressure and air at an oxygen pressure of 12.5%, corresponding to an altitude of 4400 meters. Subjects were tested by EEG, a psychomotor task, and the Romberg test. The hypoxia caused an EEG activation and an impairment of psychomotor performance. The impairment of psychomotor performance was prevented by Segolan. Hypoxia also caused a deterioration of communicativeness, concentration, energy, ego strength, and mood; these changes were prevented by Segolan. The impaired Romberg sign, occurring under placebo and hypoxia, did not occur under Segolan. The protective effect of Segolan appears to derive from a central overactivation of cortical and cardiac activity. 4 references.

001025 Castaigne, P.; Laplane, D.; Autret, A. Clinique des Maladies du Systeme Nerveux, Hopital de la Salpetriere, 47, boulevard de l'Hopital, 75634 Paris Cedex 13, France **/Experimental study of the psycho-stimulating activity of amantadine./** Etude experimentale de l'action psycho-stimulante de l'amantadine. Journal of the Neurological Sciences (Amsterdam). 28(3):345-352, 1976.

In order to study the psychostimulating activity of amantadine, experiments were conducted with Wistar rats in which polygraphic evidence was obtained. According to previous experimental and clinical data, the psychostimulating activity of amantadine on experimental sensitized models was tested. A strong action on the spontaneous sleep of rats was obtained at a dose of 10mg/kg and a less striking action in diminishing the effects of barbitol on the righting reflex of mice and in reducing the narcosis of rats induced by mebubarbital was observed. This action does not seem to be due to a release of catecholamine because the lesions produced by electrocoagulation in the ascending aminergic pathways or pretreatment by alpha-methylparatyrosine do not block it. It is suggested that there may be a nonaminergic receptor of amantadine which is different from the amphetamine receptor. 25 references. (Author abstract modified)

001026 Chadwick, Gary L. W. W. Hastings Indian Hospital, Indian Health Service, Tahlequah, OK 74464 **Psychiatric pharmacy residency and services.** Military Medicine. 141(8):537-539, 1976.

The possibility of tapping manpower within the profession of pharmacy for clinical roles in psychiatric care is discussed. To answer the question, "what does clinical pharmacy have to offer psychiatric practice?", the clinical environment in which this specialty would be practiced is examined. One instance where the pharmacist's special skills can be useful is in the history of the initial workup. The psychiatric clinical pharmacist can also provide consultation services for the prescription of psychotropic medication. Important contributions can also be made to special programs dealing with drug abuse and alcoholism. One of the most important of these gained by having a pharmacist on a mental health team is expanding the medication knowledge of patients and stage. Some functions of the pharmacist in a mental retardation center are outlined, and training programs for psychiatric pharmacy in Tennessee, Minnesota, California, and Florida are discussed. 7 references.

001027 Clift, A. D. no address **Sleep disturbance and hypnotic drug dependence.** Amsterdam, Excerpta Medica, 1975. 352 p. $35.95.

A collection of essays focusing on persons dependent on prescribed hypnotic drugs and the physiological basis of sleep is presented. Drugs discussed particularly include barbiturates, benzodiazepines, and other nonbarbiturate hypnotics. Hypnotic prescribing practices are discussed, especially the steep rise in antianxiety drug prescribing, and compared with similar practices in Australia. Also discussed are the frequently long-acting effects of many antianxiety drugs, and the implications for dependence.

001028 Cole, Jonathan O. no address **Psychotropic medications.** Hicksville, NY, Research Media, 1975. 294 p. $24.50.

A programmed instruction course on psychotropic medication is presented for nonpsychiatric personnel such as nurses, medical students, psychologists, psychiatric social workers, psychiatric aides, mental health technicians and primary care physicians. The brief descriptive text is accompanied by case studies and other illustrative examples, and a large number of multiple choice questions.

001029 Degkwitz, R. Psychiatrische Univ.-Klinik, Hauptstr. 5, 7800 Freiburg, West Germany **/Emergency cases and psychotropic drugs./** Notfalle und Psychopharmaka. Medizinische Welt (Stuttgart). 27(11):540-542, 1976.

Psychiatric emergencies that require the administration of psychotropic drugs and emergencies caused by psychotropic drugs or where their use is contraindicated are examined. Psychiatric emergencies include hyperemotional states, disturbed behavior and nocturnal unrest of all sorts; in short, any case requiring rapid sedation. Sedative drugs generally recommended include Phaenemal (phenylethylbarbiturate), Distraneurin, scopolamine combined with an alkaloid or sedative, and various neuroleptics and tranquilizers. Neuroleptics should not be used for delirium tremens or in geriatric patients. In the administration of psychotropic drugs, the effective rapidity of the method of application, the effective speed of action of the drug, and the dosage should be considered. Thymoleptics can cause disorders of central vegetative regulation, can affect extrapyramidal center, intensify other drugs, and can cause retention of urine, which may be helped with Doryl. Neuroleptics may cause extrapyramidal reactions, or akathisia (inner restlessness, repeated desire to stand and run and then lie down). Decreasing the dosage is the only solution for akathisia. Distraneurine is a good drug for treating delirium tremens, but should be used with caution because it may lead to addiction.

001030 Dehlin, Ove; Mac Dowall, Viveka; Falkheden, Thomas; Jonsson, Ulla; Palmgren, Eva; Roos, Bjorn-Erik. Langvardskliniken, Molndals Centrallasarett, Box 122, S-43122 Molndal, Sweden **/A comparison of consumption of psychopharmacological drugs./** Forbrukningen av psykofarmaka vid tva medicinkliniker och tva langvardskliniker -- en jamforelse. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 29(4):259-269, 1975.

The use of psychopharmacological drugs was compared between two medical clinics and two clinics for long-term treatment. The use of drugs was estimated in reference doses for a 1 year period. The total consumption of drugs was 23% lower at the medical clinics. The consumption of phenothiazine derivatives, buthyrophenones and thymoleptics was more than 50% higher in the clinics for long-term treatment. In the two medical clinics the benzodiazepin derivatives and barbituric acid derivatives constituted the most used psychopharmacological drugs. A 30% higher consumption of drugs was observed in the two medical clinics. The average

cost per reference dose was about the same at all four clinics. 5 references.

001031 Delaunay, J.; Guibert, S. Service de Psychotherapie, Centre Hospitalier de La Rochelle, La Rochelle, France /**A clinical trial of tropatepine chlorhydrate as a corrector of secondary neuroleptic syndromes.**/ Essai clinique du chlorhydrate de Tropatepine comme correcteur des syndromes secondaires des neuroleptiques. Annales Medico-Psychologiques (Paris). 1(1):144-147, 1976.

To examine the value of tropatepine chlorhydrate as a correction of secondary syndromes caused by the administration of neuroleptics, a study of the effects of this drug on 40 patients under treatment for neuroleptic side effects was made. Results confirm the effective action of tropatepine chlorhydrate on extrapyramidal syndromes caused by antipsycholic chemotherapy and its generally good tolerance.

001032 Deniker, M. P.; Ginestet, D.; Loo, H.; Zarifian, E. Societe Medicale des Hopitaux de Paris, Paris, France /**Is the hypothalamic hormone thyreotrope an antidepressant agent?**/ L'hormone hypothalamique thyreotrope est-elle un agent antidepresseur? Semaine des Hopitaux (Paris). 52(1):63, 1976.

At the meeting of the French Medical Society of Hospitals (May 1975), the hypothalamic hormone, thyreotrope, was discussed as an antidepressant agent. Used since 1972 and studied in double-blind procedure, thyreotrope produces a euphoria in normal subjects and an excitation in animals. It is neither a MAO inhibitor, nor an imipramine type drug nor an amphetamine type drug. Favorable results have been obtained in bipolar depression, but the drug is without effect in monopolar depression and schizophrenia. The good results obtained (20%) are superior to a placebo effect, and are obtained in several days, whereas antidepressants do not produce effects for 3 weeks. The mechanism of action could be hormonal by an action on the hypothalamic/hypophyseal axis and interrelationship with prolactin, or it could lie in interference with cerebral monoamines. (Journal abstract modified)

001033 Diamond, Herbert; Tislow, Richard; Snyder, Thoburn, Jr.; Rickels, Karl. West Philadelphia Community Mental Health Consortium, Inc., P.O. Box 8076, Philadelphia, PA 19101 **Peer review of prescribing patterns in a (CMHC).** American Journal of Psychiatry. 133(6):697-699, 1976.

A peer review and feedback system in a decentralized community mental health center is described. The program is linked to a continuing education service in psychopharmacology. It has made staff psychiatrists familiar with the state of the art and accountable for practice within its guidelines. Data are presented that confirm shifts from polypharmacy toward more appropriate use of psychotropic medications. 12 references. (Author abstract modified)

001034 Diamond, Seymour; Dalessio, Donald J.; Graham, John R.; Medina, Jose L. no address **Vasoactive substances relevant to migraine.** Springfield, IL, Charles C. Thomas, 1975. 102 p. $11.50.

Addressed to the biochemistry of migraine headache, papers presented at the 15th annual meeting of the American Association for the Study of Headache (June, 1973) are summarized. Topics include: 1) pharmacological actions of monoamines related to migraine; 2) adrenergic receptors involved in migraines pathogenesis; 3) two serotonin antagonists (LSD-25 and methysergide) and their potentiating/antogonizing effects in migraine patients; 4) the role of neurokinin, a vasodilator polypeptide; 5) histamine and its receptors' involvement in the vascular bed; 6) heparine's role in migraine's pathophysiology; 7) prostaglandin's and tyramine's role; and 8) the renin-angiotension system's involvement in migraine headaches experienced by hypertensive subjects and hemodialysis patients. The data have theoretical interest as well as therapeutic value, and neurologists, psychiatrists and internists will find it useful in treatment of migraine headache patients who are unresponsive to current conventional anti-migrainous medications.

001035 Dorfman, W. no address **Psychoactive drugs in the treatment of psychosomatic disorders.** Medicina Psicosomatica (Roma). 20(4):274, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975), paper notes that psychosomatic disorders are no longer limited to the eight personality profiles described by Flanders Dunbar or to Alexander's seven conflict situations. It is noted also, that current concepts indicate that all somatic disorders are psychosomatic (psychophysiologic) whether or not somatic pathology is present. Psychoactive drugs may be utilized concomitantly with the specific somatic therapy indicated. It is concluded that in anxiety states the utilization of minor tranquilizers can at times shorten the process of psychotherapy. Major tranquilizers are best for borderline and psychotic patients. Depressive states, often overt, but at times masked by somatic symptoms and/or disease, show varied results in different patients due to the multiple factors involved in depression. The choice of antidepressant is at times as important as the choice of physician. It is also important to evaluate the need for concomitant psychotherapy or electroshock treatment. (Author abstract modified)

001036 Estler, C.-J. Pharmakologisches Institut der Universitat Erlangen-Nurnberg, Universitatsstrasse 22, D-8520 Erlangen, Germany /**Survey and classification of psychopharmacological drugs.**/ Psychopharmaka: Ubersicht und Klassifizierung. Zeitschrift fur Allgemeinmedizin: Der Landarzt (Stuttgart). 51(9):405-417, 1975.

An overview of currently used psychopharmacological drugs is presented, together with a brief description of the chemical structure, action and side-effects of each drug. The generic name, trade name, and average daily dosage also are given for each drug. Drugs are classified according to chemical and pharmacological criteria in the following groups: ataractics, including derivatives of propandiol, benzodiazipine, diphenylmethane, and dibenzocyclooctadine; neuroleptics, including derivatives of phenothiazine, azaphenothiazine, thioxanthene, butyrophenone, diphenylbutylpiperidine, and reserpine; antidepressants, including MAO inhibitors and tricyclics; cerebral stimulants, including methylxanthine and phenylethylamine; hallucinogens, including derivatives of indol and phenylethylamine; euphoriants, including alcohol, opiates, cocaine, and barbiturates; and other substances such as lithium and sulpride.

001037 Faleni, Ricardo A. Hospital Nacional Branlio A. Moyano, Buenos Aires, Argentia /**Present and future trends in psychotropic drugs.**/ Tendencias actuales y futuras de las drogas psicotropicas. Neuropsiquiatria (Buenos Aires). 6(1):59-65, 80, 1975.

A clinical compendium of new psychotropic drugs is detailed, and the future of psychopharmacology as an approach to psychiatry is explored. The contribution of biogenic amines is acknowledged as one of the most effective means to have emerged recently in the treatment of mental abnormali-

ties. The relation between phenethylamines, amphetamines, and catecholamines are detailed. Research in antidepressant drugs is presented as a field which has experienced the most rapid progress in the last few years. Specific drugs and the treatment of schizophrenics are also described. 10 references.

001038 Fann, William E.; Wheless, Jeanine C.; Richman, Bruce W. Psychiatry Service, Veterans Administration Hospital, Houston, TX 77030 **Treating the aged with psychotropic drugs.** Gerontologist. 16(4):322-328, 1976.

Functional psychoses, affective disorders, and neuroses in the elderly are often diagnosed as senility and as such are inappropriately treated. These psychiatric entities can be effectively treated with psychotropic drugs, but drug dosage should be modified to accommodate the altered metabolism, absorption, and excretion processes of the aged. Psychiatric prognosis can be good in the elderly if careful diagnosis and drug prescription are conducted. 25 references. (Author abstract)

001039 Fields, W. S. no address **Neurological and sensory disorders in the elderly.** New York, Stratton Intercontinental, 1975. 243 p. $19.50.

A symposium on neurological and sensory disorders in the elderly is reported. Topics of discussion included neurological disorders associated with skeletal changes, pharmacological responses to drugs and interaction between drugs, and the aging person in American society. A portion of the book is devoted to sensory problems as they affect both general behavior and perception, vision and hearing. A discussion of dizziness in elderly patients is also included. Issues related to Parkinson's disease, cerebrovascular disease, and dementia are also covered.

001040 Fletcher, Donna Newcomer. Florida State University **The relationship of program participation and visitation to adaptive behavior and socialization of institutionalized mentally retarded persons. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-16519 HC$15.00 MF$8.50 123 p.

The relationship of program participation, visitation, IQ level, tranquilizers, and Down's syndrome to adaptive behavior and socialization of institutionalized mentally retarded persons was examined, using the Adaptive Behavior Scale (ABS) and the Vineland Social Maturity Scale (VSMS). Data on 896 retardates were collected and subjected to correlational analyses. The results indicated that adaptive behavior increased with program participation only for the higher IQ level residents, with the most substantial increases found for residents who did not receive tranquilizers and for Down's Syndrome retardates. Neither adaptive behavior nor socialization were related to visitation. The VSMS was more sensitive to the effects of the institutional variables than was the ABS, yielding hypotheses for experimental research in this area. (Journal abstract modified)

001041 Gilbert, Michael M.; De Sola Pool, Naomi; Schecter, Carl. 316 N.E. 14th Terrace, Miami, FL 33132 **Analgesic/calmative effects of acetaminophen and phenyltoloxamine in treatment of simple nervous tension accompanied by headache.** Current Therapeutic Research. 20(1):53-58, 1976.

The effects of acetaminophen (an analgesic), and phenyltoloxamine (a tranquilizer), alone and in combination, on tension headaches were evaluated in a double-blind, placebo controlled, multiple crossover study involving 206 patients. The effects of acetaminophen and phenyltoloxamine were additive when the drugs were given in combination as Percogesic. The only significant side-effect reported was drowsiness. (Author abstract modified).

001042 Ginestet, D.; Peron-Magnan, P.; Deniker, P. no address **Critical study of the use of long acting neuroleptics (depot neuroleptics) in France.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(4):183-186, 1976.

The indications for the use of long-acting neuroleptics in France are presented and the frequency of utilization of depot dosage forms in that country is discussed. Some psychiatrists remain reluctant to prescribe long-acting neuroleptics. Problems associated with their use are: 1) determining the relation between dosage requirements for standard neuroleptics and the corresponding depot dosage form; 2) determining dose interval for long-acting neuroleptics; and 3) the necessity of prescribing an antiparkinsonian drug to relieve side-effects. The superiority of long-acting neuroleptics may permit psychotherapy and sociotherapy to be conducted without the necessity for frequent changes of dosage or drugs. 9 references.

001043 Gisselmann, A. no address **/Barbiturate hypnotics, a too-frequent and non-soothing prescription./** Une prescription trop frequente et non anodine, les hypnotiques barbituriques. Medecine Generale (Paris). 1(2):6-14, 1975.

Pharmacology of the barbiturates is reviewed. Topics discussed include the chemical properties, pharmacological effects, enzymatic induction, classification by rate of elimination, side-effects and toxic effects, contraindications, interactions with other drugs, and risks of addiction. A list of nonbarbiturate hypnotics, which may eventually replace barbiturates, is given.

001044 Goodwin, Frederick K.; Webster, Marion H.; Post, Robert M. National Institute of Mental Health, Building 10, 4S239, Bethesda, MD 20014 **Cerebrospinal fluid amine metabolites in affective illness and schizophrenia: clinical and pharmacological studies (Unpublished paper).** NIMH, Bethesda, MD, 1975. 28 p.

The results of clinical studies and pharmacological studies dealing with amine metabolites in the cerebrospinal fluid (CSF) of depressed patients and schizophrenic patients in order to define the underlying biochemical abnormalities in these disorders are presented. These results are discussed under the following headings: 1) the origins of amines and their metabolites in the CSF; 2) the probenecid methodology in the study of CSF amine metabolites; 3) metabolite findings in affective illness; 4) metabolite findings in schizophrenia; 5) critique of existing studies; 6) relationship between metabolite data and the amine hypothesis of affective illness; 7) amine subgroups as predictors of drug response in depression; 8) amine hypothesis of schizophrenia: relationship to the metabolite data; and 9) the question of illness specificity. 103 references.

001045 Greil, W. Psychiatrische Klinik der Universitat, Nussbaumstrasse 7, 8000 Munich 2, West Germany **/Lithium prophylaxis./** Lithium-Prophylaxe. Medizinische Welt (Stuttgart). 27(11):517-522, 1976.

Lithium maintenance therapy as an effective prophylaxis against recidivism in manic-depressive cases is examined. It lessens the number and intensity of acute phases of mania and depression. Lithium salts must be administered in doses based on the lithium serum reflex of the individual patient. As soon as side-effects appear, the lithium serum level must be im-

mediately checked. Possible causes of a lithium intoxication include overdose, complicating diseases, salt poor diet, and above all combination of lithium with diuretics. Lithium is contraindicated in renal insufficiency, heart and circulatory disorders, and during the first 3 months of pregnancy. 16 references.

001046 Griffiths, Roland R.; Bigelow, George E.; Liebson, Ira. Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Human sedative self-administration: effects of interingestion interval and dose.** Journal of Pharmacology and Experimental Therapeutics. 197(3):488-494, 1976.

The variables which might influence oral sedative self-administration were studied in a residential hospital ward setting using human subjects with a documented history of drug abuse. During specified portions of the day, tokens could be earned by riding an exercise bicycle and exchanged for oral doses of either sodium pentobarbital, diazepam or ethanol. Increases in the required minimum interingestion interval from 0-30 minutes decreases the number of ingestions of sodium pentobarbital and diazepam. Increases in the dose per ingestion (30-90mg of sodium pentobarbital, 2-10mg of diazepam or 1.86-11.14g of ethanol) produce increases in the number of ingestions. The effects of the manipulated variable are similar for all of the drugs studied. It is suggested that both dose and minimum interingestion interval bear a systematic controlling relationship to the occurrence of drug self-administration behavior. 22 references. (Author abstract modified)

001047 Hara, Toshio. Department of Psychiatry and Neurology, Kitazato University School of Medicine, Japan **On the treatment of mentally disturbed college students.** In: Tokuda, Y., Perspective on school mental health. Tokyo, Nippon Seishin Eisei-kai, 1975. (p. 69-79).

A general introduction to the kinds of therapy available to the mentally ill is given in advocacy of linking such therapy directly to college mental hygiene facilities. First the history and general types of drug therapy are outlined and antiepilepsy drugs, sleeping pills, minor tranquilizers, major tranquilizers, and antidepressant drugs are listed and their general use and effects are explained. Other types of general therapy are discussed including psychoanalysis, hypnotism, autogenic training, Morita therapy, and some simple general methods are explained. Incorporation of all of these therapies in school mental hygiene programs with school authorities, doctors, and parents acting as a team is advocated.

001048 Harding, T. W.; Chrusciel, T. L. Institute for Drug Research and Control, Warsaw, Poland **The use of psychotropic drugs in developing countries.** Bulletin of the World Health Organization (Geneve). 52(3):359-367, 1975.

Psychotropic drug therapy combined with other forms of treatment provides an effective means for the control and treatment of a number of mental disorders. In developing countries, a wide range of health workers must be prepared to use psychotropic drugs if there is to be a significant improvement in mental health care. A number of problems are involved: not all mental disorders respond to drug treatment; the range of available drugs is very wide; side-effects are relatively common; patients may not take prescribed drugs regularly; and there are dangers of overuse, abuse, and overdose. Some of the problems could be overcome by: 1) focusing on a limited number of conditions of public health importance; 2) establishing a clear policy as to which drugs should be available at various points in the health service and limiting the range of such drugs; 3) adopting a more flexible system of task sharing in psychotropic drug therapy; 4) coordinating training programs; and 5) setting up a central policy body concerned with mental health in health ministries. 27 references. (Author abstract)

001049 Heinrich, K. Psychiatr. Klinik der Univ., Bergische Landstr. 21, 4000 Dusseldorf 12, West Germany /**Psychoactive drugs in medical practice: the present stage of development.**/ Psychopharmaka in der Praxis -- Stand der Entwicklung. Medizinische Welt (Stuttgart). 27(11):499-507, 1976.

The major psychoactive drugs in current use are reviewed, including neuroleptics, thymoleptics, lithium preparations, and tranquilizers, together with their indications, contraindications, and side-effects, to familiarize nonpsychiatrist physicians with their use. Five different tables are devoted to mild, medium, strong, very strong, and maintenance therapy neuroleptics, showing trade names (German), generic names, chemical groups, major indications, clinical dosage, outpatient dosage, and possible side-effects. Similar single tables are included for thymoleptics, lithium preparations, and tranquilizers. The indications for usage, side-effects, and therapeutic goals also are discussed for each group of drugs. With a sensitive awareness of the possible dangers of side-effects and a sober estimation of therapeutic expectations, the role of the physician in prescribing psychoactive drugs is irreplaceable. For example, schizophrenics who require years of treatment after release from the hospital, and patients suffering from endogenous depressions can best be served by their family physician.

001050 Hesbacher, P.; Stepansky, P.; Stepansky, W.; Rickels, K. Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104 **Psychotropic drug use in family practice.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(2):50-60, 1976.

In an attempt to assess the precision of an illness/treatment fit between dispensing and actual need for psychotropic medication, approximately 200 consecutive patients above age 18 from each of 7 general practices were surveyed and classed as: 1) presently receiving psychotropic therapy; 2) previously receiving drug treatment; and 3) never having received such treatment. Emotional problems were rated by both the examiner and the patient. Of the 560 patients with emotional problems in the study 51% had not received psychotropic medication, 21% had previously received psychopharmacological therapy, and 28% presently were receiving drug therapy. Thus almost half (49%) of the patients with emotional problems had received psychotropic drugs during the past 2 years, but less than a third (28%) were still receiving drug therapy. The results also showed the following: 1) emotionally ill patients in family practice tended to be female; 2) fewer Blacks than whites revealed emotional problems; 3) patients presently receiving drug therapy proved significiantly older than those not receiving drug therapy; and 4) patients currently receiving drugs tended to be lowest in social class. The study showed that private general practitioners make conservative use of psychotropic drugs, insofar as patients were seldom dispensed medication in the absence of emotional problems, and the presence of emotional problems frequently was not accompanied by dispensing of medication. 27 references.

001051 Hollister, Leo E. Veterans Administration Hospital, Palo Alto, CA **Improved clinical screening of phrenotropic drugs.** Psychopharmacology Bulletin. 12(3):78-79, 1976.

A series of studies is conducted in which antipsychotic drugs, antidepressant drugs and antianxiety drugs are screened and drugs are used as tools for better understanding of the nature of mental disorders. The emphasis is on exploratory clinical trials of new approaches to treatment. Thyrotropin releasing hormone (TRH) is reported to be an ineffective treatment for depression. Some patients with depression show blunted pituitary ease of thyrotropin from TRH stimulation although the degree of pituitary response does not correlate with the degree of depression. TRH aggravates paranoid schizophrenics, indicating an action on the CNS. Butaclamol is an effective antipsychotic drug but has a great tendency to produce motor disturbances. Initial responses of patients with tardive dyskinesia to loading with choline have been promising but the effects may be of greater theoretical importance than practical importance.

001052 Hollister, Leo E. Stanford University School of Medicine, Palo Alto, CA 94304 **Psychopharmacology in its second generation.** Military Medicine. 141(6):371-374, 1976.

An overview of the present status and future of the field of psychopharmacology is presented. Its role in the amelioration of major mental disorders and the clarification and improvement of brain function is discussed. Psychotic disorders, drug and alcohol abuse, mental retardation and senility, behavioral control, sexual function, sleep, and manipulation of traumatic psychological events are subjects within the realm of the psychopharmacologist. 18 references.

001053 Jaroszynski, Jan. I. Kliniki Psychiatryczna Instytutu Psychoneurologicznego, Warsaw, Poland **/Proposed guidelines for conducting clinical trials of psychotropic drugs (replicated)./** Propozycje w sprawie zasad przeprowadzania badan klinicznych lekow psychotropowych (odtworczych). Psychiatria Polska (Warszawa). 10(1):29-32, 1976.

Principles for conducting clinical trials of new psychotropic drugs are suggested, including criteria for use, where responsibility for introduction of a drug lies, who should carry out drug trials, and what information the patient should be given about a drug. It is concluded that no drug should be used unless it is safe, its effects are fully known, and it is in accordance with ethical and legal standards.

001054 Joss, E. Frohbergweg 3, CH-3012 Bern, Switzerland **/Enuresis./** Enuresis. Therapeutische Umschau (Bern). 33(3):147-151, 1976.

The incidence, and the pharmacotherapy and aversion therapy of enuresis in school age children are discussed. The incidence of enuresis is about 10% in school children and 1% in adults. It occurs more frequently in boys, and about 85% of cases are primary. In most cases, no cause can be found. Factors predisposing the child to enuresis are occasionally hereditary, but sociological and poor family relationships or psychological factors rarely apply. Urological and neurological disorders, and urinary tract infections frequently accompany enuresis. Some tricyclic antidepressants have been shown to be effective in treatment of enuresis; they probably act by an anticholinergic effect directly on the bladder. About 40% of patients respond to these drugs. The most effective therapy is the aversive conditioning system in which urine makes an electrolytic contact between two electrodes, activating an alarm clock. Applied only to children 7 years and older, this system usually produces results within 6 to 8 weeks in 65% to 100% of cases. Antidepressants are tried in cases in which the electrolytic alarm has failed. 21 references.

001055 Kupfer, David J.; Foster, F. Gordon; Reich, Louis; Thompson, Kenneth S.; Weiss, Brian. University of Pittsburgh Western Psychiatric Institute and Clinic, Pittsburgh, PA 15261 **EEG sleep changes as predictors in depression.** American Journal of Psychiatry. 133(6):622-626, 1976.

A study of 18 depressed patients to determine whether EEG sleep measurements might provide a predictive tool for response to antidepressant medication was conducted. Data indicate that although the sedative characteristics of amitriptyline did not differentiate good responders from poor responders until the third week of drug treatment, the good responders showed significant increases in REM latency, decreases in REM sleep time, decreases in REM sleep percent, and decreases in REM activity after only 2 nights of drug treatment. 25 references. (Author abstract)

001056 Kuran, Wlodzimierz. I Klinika Neurologiczna Instytutu Psychoneurologicznego, Al. Sobieskiego 1/9, 02-957 Warszawa, Poland **/Therapeutic application of L-dopa./** Terapeutyczne zastosowania L-dopy. Wiadomosci Lekarskie (Warszawa). 28(17):1467-1472, 1975.

Methods and principles of the therapeutic use of L-dopa are discussed in relation to nervous, endocrine, dermatologic and other disorders. L-dopa, used in the treatment of disorders of the extrapyramidal system, is particularly effective in cases of parkinsonism, where 70% of the patients improve considerably after 1-2 years of treatment. L-dopa stimulates the production of neurohormones. The drug has been used in the treatment of Cushing's disease, anorexia nervosa, and impotence. L-dopa plays an important part in catecholamine and melanin synthesis. Improvements have also been observed in several somatic diseases. 58 references.

001057 Lehmann, Heinz E. Douglas Hospital, Montreal, Quebec, Canada **Comprehensive clinical studies of psychoactive drugs.** Psychopharmacology Bulletin. 12(3):79, 1976.

An investigation is carried out to determine the effectiveness of psychoactive drugs in geriatric patients, neurotics, depressivess and schizophrenics as measured through observable changes in behavior, perceptual mental alertness tests, and biochemical studies. After screening in one or more patient groups, drugs appearing to exert a positive therapeutic effect are studied further in placebo controlled studies or in controlled comparison with a drug of known therapeutic value. Benzoctamine, etafenoxin, lorazepan and trazodone produced sufficient beneficial effects in neurotic patients to warrant further study. Lorazepam was least beneficial to patients and etafenoxin produced the most side-effects. Clomipramine proved to be an effective antidepressant and may have therapeutic activity in obsessive-compulsive manifestations. Ludiomil has significant antidepressant activity which may be equal to or superior to that of imipramine. Trazodone is superior to placebo, and at least as effective as amitryptilene in treating depression. Nomifensin relieves symptoms of depression and hostility in patients with affective disorders. Thyrotropin releasing hormone (TSH) appears to be superior to placebo in alleviating sleep disorders and anxiety/depression factor scores on the Hamilton Rating Scale. In schizophrenics, clomacran is an effective drug; pimozide is as effective as trifluoperazine in maintenance therapy of chronic patients and thiothixene is as effective as chlorpromazine. Penfluridol is superior to placebo in chronic schizophrenics only in psychometric test performance but butaclamol produces significant clinical improvement as well as improved psychometric test performance. In geriatric patients, trazodone alleviates affective psychopathology and possibly some organic psychopathology

but doxepin and diazepam fail to significantly improve clinical performance.

001058 Levine, Jerome. Psychopharmacology Research Branch, DERP, NIMH, Rockville, Md 20857 **Toward the development of contemporary standards for the pharmacotherapy of mental disorders -- prologue and epilogue. (Unpublished paper).** Psychopharmacology Research Branch, DERP, NIMH, 1976. 8 p.

The proposed prologue and epilogue to a volume entitled "Toward the Development of Contemporary Standards for the Pharmacotherapy of Mental Disorders", resulting from a session held at the Second Tulane Medical Symposium on Principles and Techniques of Human Research and Therapeutics, is presented. The volume is an attempt to describe the state of the art with regard to the pharmacotherapy of mental disorders. The approach was to select the core psychiatric disorders and to describe their treatment by pharmacological means. Professionally developed expressions of a range of acceptable treatment approaches are discussed. Included in the volume is an attempt to blend pharmacotherapy with the more traditional psychotherapeutic treatment approaches and somatic treatment approaches. Chapters on the treatment of schizophrenia, psychotic disorders, neurotic depressive disorders, manic-depressive disorders, anxiety, and phobic states attempt to provide the clinician with recommendations based on clinical research findings. The pharmacotherapy of mental disorders of children is also discussed. Other topics included are common errors in the treatment process with drugs as they relate to efficacy, side-effects and toxicity, a view of the place and status of pharmacotherapy as one tool available to the practitioner, and some ideas of how the treatment technique could be improved.

001059 Macias Quintana, Maria del Carmen. Hospital Braulio A. Moyano, Buenos Aires, Argentina **/Toxicomania in hallucinogenic drugs./** Toxicomanias drogas alucinogenas. Neuropsiquiatria (Buenos Aires). 6(1):36-48, 1975.

Reasons for drug use as a recent social phenomenon are explored. The characteristics, history, effects and side-effects, and change effects that hallucinogenic drugs produce are described. Therapetic applications are also detailed. Among the drugs described are: LSD, adenochromes, bufotenine, hallucinogenic mushrooms, synthetic hallucingoens, peyote and mescaline, and marihuana. 36 references.

001060 Marcus, Julius. Nassau County Medical Center, East Meadow, NY **Dosage for antipsychotic drugs.** New England Journal of Medicine. 295(3):174, 1976.

Dosage considerations for the average schizophrenic patient are discussed in a letter to the editor. Although clinically the physician is concerned with patients who are chronically assaultive, disruptive, and who terrorize the staff and other patients, drug megadoses can restore patient calm and staff functioning. A therapeutic dose can be substituted at this point by intramuscular administration.

001061 Murphy, Dennis L. NIH Clinical Center, Bldg 10, Room 3S229, Bethesda, MD 20014 **Monoamine oxidase, monoamine oxidase inhibiting drugs and human behavior (Unpublished report).** Laboratory of Clinical Science, NIMH, 1976. 23p.

Evidence suggesting some associations between monoamine oxidase (MAO) activity and human behavior is presented. Studies on human brain MAO are reviewed as well as recent studies of human platelet MAO. Evidence indicating that drugs as well as genetic, nutritional and hormonal factors can influence the activity of this enzyme and possibly its relationships with human behavior is discussed. The literature which provides some hypotheses about the behavioral effects of MAO inhibiting drugs is also reviewed. 113 references.

001062 no author. no address **Alternatives to levodopa.** British Medical Journal (London). 1(6019):1169-1170, 1976.

The therapeutic effects, side-effects, mechanism of action, and possible causes of treatment failure of levodopa in patients with Parkinson's disease is reviewed. The therapeutic effects, side-effects and mechanism of action of four dopamine agonists which may be useful alternatives to levodopa (i.e. piribedil, apomorphine, and the ergot alkaloids bromocriptine and lergotrile) are discussed. It is suggested that the other dopamine agonists are not likely to be useful in most conditions associated with levodopa failure. 16 references.

001063 Ott, Jonathan. Instituto de Investigaciones Biomedicas, Universidad Nacional Autonoma de Mexico, Apartado Postal 70228, Mexico 20, D.F. **Psycho-mycological studies of Amanita -- from ancient sacrament to modern phobia.** Journal of Psychedelic Drugs. 8(1):27-35, 1976.

Following a review of the history, chemistry, and pharmacology of Amanita muscaria and its chemotaxonomic relatives, and its role in religious cults, the modern use of the psychotropic Amanita species is described with the subjective effects of Amanita intoxication, and the inhibiting phobia which restricts modern recreational use of these mushrooms. Modern amanitaphobic attitudes probably derive from ancient cult taboos and from the visual symbol as "the ancient toadstool." Five potentially deadly Amanita species which contain alpha-amanitin and amatoxins are listed. 55 references.

001064 Pare, C. M. B. Department of Psychological Medicine, St. Bartholomew's Hospital, London EC1A 7BE, England **Unwanted effects of long-term medication in schizophrenia and depression.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(4):187-192, 1976.

The types of side-effects occurring with prolonged use of various psychoactive drugs are mentioned and the frequency of occurrence and significance of these adverse effects are discussed. Benzodiazepines may produce: 1) drowsiness; 2) a paradoxical increase in hostility, especially in frustating situations (observed with chlordiazepoxide and diazepam but not with oxazepam); and 3) possible habitation, expecially with prolonged use of very high doses. Except for sedation, these side-effects occur very rarely and the benzodiazepines are considered very safe. Major tranquilizers may produce: 1) pigmentation in various structures of the eye (especially of the cornea and lens by chlorpromazine and of the retina by thioridazine), with high doses; 2) galactorrhea and decreased gonadal functioning in both males and females, probably due to increased blood levels of prolactin; and 3) tardive dyskinesias. The pathological cause of the tardive dyskinesias is not confirmed but may be related to cell degeneration in the substantia nigra, cholinergic influences, or a reduction in the number of gabaminergic neurones in the basal ganglia. Tricyclic antidepressant therapy may be associated with increases in weight and with effects on the heart. Small doses of these antidepressants increase blood pressure, heart rate, cardiac contractility and coronary artery blood flow; larger doses decrease these measurements. Minor electrocardiographic changes also occur. Cardiotoxicity is especially associated with overdosage and the tendency of depressed patients to use

medication in suicide attempts must be considered. 46 references.

001065 Parent, M.; Toussaint, Ch. no address **/Cerebral neurotransmission and psychotropic drugs./** Neurotransmission cerebrale et psychotropes. Feuillets Psychiatriques de Liege (Liege). 8(3):233-251, 1975.

Present data from research on the biochemistry of the brain and the mechanism of action of psychotropic drugs on the central nervous system are reviewed. Topics discussed include: the elements of cerebral biochemistry; the synthesis and difference in structure between catecholamines and indolamines; the catabolism of catecholamines and the role of monoamine oxidase (MAO); catecholamines as chemical mediators; the role of acetylcholine in cerebral neurotransmission; anatomical localization of central monoaminergic neurons; the mechanism of action of neuroloptics, antidepressants, tricyclic antidepressants, sulpiride and lithium; the biochemical basis for mental illness, in particular schizophrenia and cyclophrenia; and the relationship between various biogenic amines and melancholia or mania. 15 references.

001066 Perris, C. Umea University, Department of Psychiatry, S-901 85 Umea, Sweden **Indications for long-term pharmacological treatment of schizophrenic syndromes.** Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 9(4):149-158, 1976.

Differences of opinion concerning the hypotheses which might motivate a long-term pharmacological treatment of schizophrenia are presented and their possible implications discussed. A short review of factors which might influence the decision for long-term pharmacological therapy is also presented. Recommendations for appropriate management of long-term psychopharmacological treatment are suggested. 35 references. (Author abstract modified)

001067 Rees, W. L. no address **The advantages and disadvantages of psychotropic drugs in the treatment of psychosomatic disorders.** Medicina Psicosomatica (Roma). 20(4):280, 1975.

Presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975), paper presents a critical assessment of the value and limitations of various psychotropic drugs in the treatment of psychosomatic disorders. Consideration is given to the limited role offered by neuroleptic drugs, including phenothiazines, rauwolfia alkaloids and benzoquinolizines, thioxanthines, butyrophenones, diphenyl butyl piperidines, dibenzothiazepines, and benzamides. References are made to the dangers and disadvantages of hypnosedative drugs, including the barbiturates, as well as the valuable role played by the benzodiazepines when prescribed judiciously. The pros and cons of the monoamine inhibitor drugs are discussed, and various indications for the use of tricyclic antidepressants in the management of various psychosomatic disorders are explored. The role of adrenergic receptor drugs, including blockers, is considered, as is the use of various hormones for male and female sexual disorders. Finally, the place of lithium in thyrotoxicosis is reviewed. (Author abstract modified)

001068 Renard, P.; Pascaud, M. no address **/Lithium treatment. Some data and recent perspectives./** Traitements au lithium: quelques donnees et persepctives recentes. Revue de Neuropsychiatrie de l'Ouest (Rennes). 12(50):57-66, 1975.

The indications and side-effects of lithium are reviewed. Lithium is contraindicated or should be used with caution in advanced age, diabetes, goiter and pregnancy. Of 150 children born whose mothers were treated with lithium during the first 3 months of pregnancy, 16 had malformations, of which 12 were cardiovascular. Side-effects from lithium were asthenia, diminished libido, increased emotionality, difficulty in memory and cognition, decrease in creativity, palpebral pain, diminished interest, reduced attention, tremors, polyuria/polydipsia, digestive problems, diarrhea, electrolyte problems, gastric pain, nausea, vomiting, flatulence, thyroid insufficiency, weight gain, leukocytosis, acne, psoriasis, exophthalmia, epilepsy, dyskinesia, tics, and EKG modifications. Results with lithium treatment were excellent in 1/4, good in 1/2, and mediocre in 1/4 of the patients who responded; 10% did not respond. Psychiatric indications for lithium are mania, hypomania, and affective psychoses. Nonpsychiatric indications are hyperthyroidism, Huntington's chorea (lithium + haloperidol), L-dopa dyskinesia, and spasmodic torticollis.

001069 Schindler, Raoul. Bennogasse 8, A-1080, Wien, Austria **/Prevention of recidivism in the age of long-acting neuroleptics and social psychiatry./** Rezidivverhutung im Zeitalter von Depotneuroleptika und sozialer Psychiatrie. Nervenarzt (Berlin). 47(5):347-350, 1976.

Trends in the treatment of psychoses are discussed on the basis of practical experience in Austria with a long-acting neuroleptic (Dapotum D: fluphenazine decanoate). Intensive therapy with neuroleptics has enabled a considerable reduction in the inpatient treatment period. A program of treatment is outlined which permits release from hospital within 3 weeks, the legally required period for elimination of incompetent behavior. In this way, major responsibility for the management of psychiatric treatment and improvement of social crises is shifted to the followup therapy phase, which still is somewhat neglected and depends mainly on nonspecialist physicians. Progress in the area of long-acting neuroleptics has enabled strict control of aftercare procedures, but this places total responsibility on the physician. Forced stabilization of a psychosis with chemotherapy is achieved at the cost of a certain amount of social adaptation achievable through psychotherapeutic assistance, and vice versa. To counteract a possible unilateral bias on the part of the physician, a program of therapy of schizophrenia is presented which strives for an optimal balance of pharmacotherapeutic and psychotherapeutic phases of treatment on the basis of insight into the personality deviation. 22 references.

001070 Schmidt, R. T.; Lee, R. H.; Spehlmann, R. VA Lakeside Hospital, 333 East Huron Street, Chicago, IL 60611 **Comparison of dantrolene sodium and diazepam in the treatment of spasticity.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 39(4):350-356, 1976.

The effects of dantrolene sodium and those of diazepam were compared in order to study benefits and side-effects, and to refine indications for each agent in the treatment of spasticity. The comparison consisted of a double-blind crossover study of 42 patients with spasticity due to stable multiple sclerosis. It was found that both drugs reduced the findings of spasticity, clonus, hyperreflexia, and complaints of muscle stiffness and cramping. Neither drug improved hand coordination, hand speed, foot speed, or walking speed, but high doses of dantrolene improved station stability. Each drug had different side-effects which suggest indications and contraindications for its use in spastic patients. Side-effects reported included weakness in extremities, drowsiness, gait deterioration,

deterioration of hand coordination, hand speed, station stability, and walking speed, incoordination of motor elements, and imbalance. Observations offer some guidance in selection of a suitable drug and dosage for treating spasticity in individual patients with multiple sclerosis. 29 references. (Journal abstract modified)

001071 Schneider, H. Bismarckstr. 6, 7050 Waiblingen, West Germany **/Administration of psychotropic drugs from the standpoint of the general practitioner./** Einsatz der Psychopharmaka aus der Sicht des Allgemeinarztes. Medizinische Welt (Stuttgart). 27(11):542-545, 1976.

The administration of psychotropic drugs from the standpoint of the general practitioner is examined. In a general practitioner's office about 40% of all patients are either mentally ill or have symptoms of mental illness in addition to their physical problems. Usually it is a matter of psychovegetative syndromes, functional syndromes or endogenous depressions -- i.e. psychosomatic or purely somatic disorders. Therefore, every practicing doctor should familiarize himself with psychotropic drugs. (Journal abstract modified)

001072 Schou, Mogens. Aarhus University, Psychiatric Hospital, Risskov, Denmark **A bibliography on the biology and pharmacology of lithium -- Appendix II (Part III).** Psychopharmacology Bulletin. 12(3):86-99, 1976.

A bibliography of published papers in textbooks and journals throughout the world dealing with the biologic and pharmacologic effect of lithium is presented. This is the third and last part of the second appendix to a bibliography originally published in 1969.

001073 Schultes, Richard Evans. Botanical Museum, Harvard University, Cambridge, MA 02138 **Indole alkaloids in plant hallucinogens.** Journal of Psychedelic Drugs. 8(1):7-25, 1976.

A botanical survey of New and Old World psychoactive flora with 9 illustrations and eleven photographs describes chemotaxonomic relationships between the principal indole alkaloids in hallucinogenic plants. These are: n,n-dimethyltryptamine; psilocybine; 5-methoxy-n,n-dimethyltryptamine; harmine; ibogaine; and d-lysergic acid amide. 71 references.

001074 Shader, Richard I. Harvard Medical School, Cambridge, MA **Manual of psychiatric therapeutics: practical psychopharmacology and psychiatry.** Boston, Little, Brown, 1975. 362 p. $8.95.

Intended for admitting room use as a primer on the use of psychotherapeutic drugs, the management of psychiatric patients under crisis conditions is addressed in 20 chapters. In outline form, topics range from psychotropic drugs in the general hospital to hypnosis to management of violent patients and practical dietary considerations.

001075 Takamuro, Masaichiro. National Konodai Hospital, Japan **Theory of treatment -- pharmacotherapy.** In: Yokoi, S., Schizophrenia. Tokyo, Igaku Shoin, 1975. (p. 241-261).

The history and theory of psychopharmacologic treatment of schizophrenia over the past 20 years is reviewed. Various psychotropic drugs are classified and identified as to their overall characteristics according to Delay's scheme: psycholeptics, psychoanaleptics, and psychodysleptics. The chemical structures of typical drugs are shown in diagram. Major drug types are then explained (their uses and effects) in turn: phenothiazine, reserpine, and butyrophenone. The general effectiveness of these drugs is detailed, and systems for evaluating their effectiveness are introduced. Individual clinical applications of the various drugs, and evaluations of their side-effects are not covered. In conclusion, evaluation of drug therapy from several aspects (social, medical, and with regard to their value vs. harmful side-effects) is urged. 33 references.

001076 Vinar, O. Institute of Psychiatry, Prague 8, Bohnice, Czechoslovakia **Psychopharmacology research ward. Ten years' experience.** International Pharmacopsychiatry (Basel). 11(1):32-42, 1976.

That the differences between the results of controlled clinical research and the experiences of the practitioners can be attributed to a certain extent to the artificiality of the setting in which controlled studies are performed is evaluated. The system developed in the wards of the Department of Psychopharmacology of the Institute of Psychiatry in Prague as an attempt to overcome some of these difficulties is reported. Certain similarities exist between this system called continuous controlled trial and silent trial proposed by Ross et al, and the main characteristics of the system are: 1) all patients admitted to the ward are assigned to the trial without exception; 2) the trial goes on continuously without interruption for more than 10 years; 3) the patients do not know the quality of drugs administered nor do they realize any difference between this research setting and the usual routine treatment. It is concluded that the advantages of this system are: reduction of artificiality; the possibility to perform early clinical trials in controlled conditions and to shorten the usual three phase testing of a new drug; the possibility to perform long-term, longitudinal studies with individual patients admitted several times in double-blind conditions. 23 references. (Author abstract modified)

001077 von Eiff, A. W. no address **The planning of a therapeutic comparison in psychopharmacology.** Medicina Psicosomatica (Roma). 20(4):274-275, 1975.

Paper presented at the Third Congress of the International College of Psychosomatic Medicine (Rome, September, 1975) cautions that it is desirable to check subjective responses, as well as objective responses of subjects in drug trials. Because of the difficulty of assessing objective symptoms in psychopharmacological trials, it is necessary to plan the trial in a way that allows the results to be seen as proof of the effects of the drugs. Proposals for such a therapeutic trial are made. In checking subjective responses the questionnaire is recommended as the best method. It is added that therapeutic effects, as well as subjectively felt side-effects, should be taken into consideration. (Author abstract modified)

001078 Wauquier, A. Department of Pharmacology, Janssen Pharmaceutica, Research Laboratoria, B-2340, Beerse, Belgium **The influence of psychoactive drugs on brain self-stimulation in rats: a review.** In: Wauquier, A., Brain-stimulation reward. New York, North-Holland Publishing, 1975. 622 p. (p. 124-170).

In a paper presented at the First International Conference on Brain Stimulation Reward, Beerse, Belgium, 1975, research on the influence of psychoactive drugs on intracranial self-stimulation (ICSS) in rats is reviewed, including the effects of CNS stimulants, cholinergics and anticholinergics, hallucinogens, anticonvulsants, minor tranquilizers, narcotic analgesics, antidepressants, hypnotics and sedatives, and neuroleptics. The data indicate that: 1) psychoactive drugs interfere with ICSS through action on motor or sensory functions and/or produce their effects through action on the reinforcing

process; 2) the effects do not generally differ from those of other forms of operant behavior, whether positively or negatively motivated; 3) some effects can be viewed in terms of drug interference with performance ability; 4) the dopaminergic nigrostriatal system is part of the substrate of the motor output and is linked to structures subserving sensorimotor integrative functions; 5) sensitizing and threshold reduction of the reinforcement substrate could be the mechanism by which narcotic analgesics and CNS stimulants enhance the ICSS response rates; 6) CNS stimulants, narcotic analgesics, and neuroleptics probably do not have a specific effect on reward; and 7) the effects of cholinergics, anticholinergics and minor tranquilizers are difficult to explain based on impact on noradrenergic or dopaminergic ICSS substrate. 289 references.

001079 Weiner, J.; Schumacher, G. E. no address **Psychotropic drug knowledge.** American Journal of Hospital Pharmacy. 33:237, 1976.

Familiarity with psychotropic drug therapy was tested in eight groups of health care practitioners. All were from the Detroit area, except for the group of psychiatric clinical pharmacists who actually practiced throughout the U.S. Participants read three case histories (covering schizophrenia, depression, and mania) and answered related questions regarding diagnosis, drug selection, side-effects, drug interactions, and clinical drug judgment. The psychiatric clinical pharmacists scored highest (85%), but this was not significantly different from the score of psychiatrists (77%). There was a significant difference between these two groups of practitioners and the remaining six groups. Hospital pharmacists, both those practicing in mental institutions and those in nonmental institutions, were ranked next (47% and 48%). Nonpsychiatrists physicians ranked fifth (46%), followed by nurses in mental health institutions (38%), community pharmacists (34%), and nurses in nonmental institutions (22%). These results suggest that clinical pharmacists with special training in psychotropic drug therapy and patient assessment may be capable of effectively managing the drug therapy of patients in mental health institutions and affiliated clinics. However, patients receiving psychotropic drug therapy in nonpsychiatric hospitals and in generalized ambulatory and community medicine environments are being served by physicians, nurses, and pharmacists whose knowledge of psychotropic drug therapy may be inadequate. (Journal abstract)

001080 Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC **Biochemistry and schizophrenia (Part IV): the neuroleptics -- their mechanism of action: a review of the biochemical literature.** Psychopharmacology Bulletin. 12(3):5-50, 1976.

The literature on the biochemical effects of the neuroleptics used to treat schizophrenia is partially reviewed. Among the topics covered are: 1) plasma drug concentrations and brain drug concentrations required to produce clinical biochemical effects and experimental biochemical effects; 2) relative clinical potency of various neuroleptics; 3) tolerance to continued administration; 4) interaction between neuroleptics and anticholinergic drugs; 5) effects of neuroleptics on dopamine and other catecholamines; 6) effects of neuroleptics on histamine; 7) effects of neuroliptics on acetylcholine; 8) effects of neuroleptics on gamma-aminobutyric acid (GABA) and glutamic acid; 9) effects of neuroleptics on brain protein synthesis; 10) effects of neuroptics on cell membranes; 11) effects of neuroleptics on adenosine diphosphate (ADP), adenosine triphosphatase (ATPase) and brain metabolism; and 12) the hyperglycemia inducing effects of neuroleptics. The relevance of published research and the types of research needed to understand the causes of schizophrenia and to provide more effective therapy for this condition is discussed. 281 references.

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